(FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, BIOSIS, MEDICONF'
ENTERED AT 14:10:18 ON 15 JUL 2002)
DEL HIS

L1 206845 S RESTENOSIS OR STENOSIS
L2 630 S L1 AND (VEGF? OR (VASCULAR ENDOTHELIAL))
L3 358 DUP REM L2 (272 DUPLICATES REMOVED)
L4 269 S L3 AND (GENE OR DNA OR DEOXY? OR TRANS? OR VIR? OR VECTOR)
L5 269 FOCUS L4 1-
L6 96 S L5 AND PY<=1998
L7 1 S L6 AND (VEGF-D OR VEGF-C)
L8 4 S L3 AND ALITALO?/AU
L9 4 DUP REM L8 (0 DUPLICATES REMOVED)

=> d an ti so au ab pi l9 1-4

L9 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2002 ACS
AN 2002:444386 CAPLUS
DN 137:19390
TI **VEGF**-C polypeptides, polynucleotides and anti-**VEGF**-C antibodies for diagnosing and treating endothelial or angiogenic diseases
SO U.S., 71 pp., Cont.-in-part of U.S. 6,245,530.
CODEN: USXXAM
IN **Alitalo, Kari**; Joukov, Vladimir
AB The invention discloses **VEGF**-C, a polypeptide ligand for Flt4 receptor tyrosine kinase (**VEGFR**-3), polynucleotides encoding them, and antisense oligonucleotides for diagnosis, therapy and drug screening use. The invention also provides monoclonal and polyclonal antibodies that are reactive with **VEGF**-C for diagnostic application to monitor angiogenesis, vascularization, lymphatic vessels and their disease states, wound healing, or certain hematopoietic or leukemia cells, and for blockade or activation of Flt4 receptor. The ligand and antibody may be coupled to supermagnetic , paramagnetic, electron dense, echogenic, or radioactive agent for imaging.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 6403088	B1	20020611	US 1996-601132	19960214
US 6221839	B1	20010424	US 1995-510133	19950801
US 6245530	B1	20010612	US 1996-585895	19960112
CA 2228248	AA	19970213	CA 1996-2228248	19960801
WO 9705250	A2	19970213	WO 1996-FI427	19960801
WO 9705250	A3	19970410		
W: AU, CA, CN, JP, NO, NZ, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9666169	A1	19970226	AU 1996-66169	19960801
AU 711578	B2	19991014		
EP 842273	A2	19980520	EP 1996-925768	19960801
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11510689	T2	19990921	JP 1996-507262	19960801
WO 9833917	A1	19980806	WO 1998-US1973	19980202
W: AU, CA, CN, JP, NZ, US, US, US, US, US, US, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				

L9 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2002 ACS
AN 2000:290851 CAPLUS
DN 132:318341
TI Use of **VEGF**-C or **VEGF**-D gene or protein to prevent **restenosis**
SO PCT Int. Appl., 61 pp.
CODEN: PIXXD2
IN Yla-Herttuala, Seppo; **Alitalo, Kari**; Hiltunen, Mikko O.; Jeltsch, Markku M.; Achen, Marc G.
AB The present invention provides materials and methods for preventing **stenosis** or **restenosis** of a blood vessel using **Vascular Endothelial** Growth Factor C (**VEGF**-C) and/or **Vascular Endothelial** Growth Factor D (**VEGF**-D) genes or proteins. A medical device designed to contact a surface of a blood vessel in the course of surgery to treat **stenosis** of the blood vessel is also claimed, the device characterized by an improvement comprising integrating into the device a

compn. effective to prevent **restenosis**, said compn. comprising at least one anti-**restenosis** agent selected from the group consisting of a **VEGF**-C polynucleotide, a **VEGF**-C polypeptide, a **VEGF**-D polynucleotide, and a **VEGF**-D polypeptide. The medical device is selected from the group consisting of intravascular stents, intravascular catheters, extravascular collars, elastomeric membranes adapted to cover a surface of an intravascular stent or catheter, and combinations thereof. Also claimed is a kit for treating **restenosis** comprising a container holding at least one anti-**restenosis** agent of the invention and a label attached to or packaged with the container, the label describing use of the compd. for prevention of **restenosis** of a blood vessel. The kit further comprises a medical device of the invention.

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000024412	A2	20000504	WO 1999-US24054	19991026
	WO 2000024412	A3	20000803		
	W: AU, CA, CN, JP, NO, NZ				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 1126870	A2	20010829	EP 1999-956559	19991026
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	NO 2001002017	A	20010626	NO 2001-2017	20010424

L9 ANSWER 3 OF 4 MEDLINE
AN 2000507205 MEDLINE
TI Intravascular adenovirus-mediated **VEGF**-C gene transfer reduces neointima formation in balloon-denuded rabbit aorta.
SO CIRCULATION, (2000 Oct 31) 102 (18) 2262-8.
Journal code: 0147763. ISSN: 1524-4539.
AU Hiltunen M O; Laitinen M; Turunen M P; Jeltsch M; Hartikainen J; Rissanen T T; Laukkanen J; Niemi M; Kossila M; Hakkinen T P; Kivela A; Enholm B; Mansukoski H; Turunen A M; **Alitalo K**; Yla-Herttuala S
AB BACKGROUND: Gene transfer to the vessel wall may provide new possibilities for the treatment of vascular disorders, such as postangioplasty **restenosis**. In this study, we analyzed the effects of adenovirus-mediated **vascular endothelial** growth factor (**VEGF**)-C gene transfer on neointima formation after endothelial denudation in rabbits. For comparison, a second group was treated with **VEGF**-A adenovirus and a third group with lacZ adenovirus. Clinical-grade adenoviruses were used for the study. METHODS AND RESULTS: Aortas of cholesterol-fed New Zealand White rabbits were balloon-denuded, and gene transfer was performed 3 days later. Animals were euthanized 2 and 4 weeks after the gene transfer, and intima/media ratio (I/M), histology, and cell proliferation were analyzed. Two weeks after the gene transfer, I/M in the lacZ-transfected control group was 0. 57+/-0.04. **VEGF**-C gene transfer reduced I/M to 0.38+/-0.02 (P:<0.05 versus lacZ group). I/M in **VEGF**-A-treated animals was 0.49+/-0.17 (P:=NS). The tendency that both **VEGF** groups had smaller I/M persisted at the 4-week time point, when the lacZ group had an I/M of 0.73+/-0.16, the **VEGF**-C group 0.44+/-0.14, and the **VEGF** -A group 0. 63+/-0.21 (P:=NS). Expression of **VEGF** receptors 1, 2, and 3 was detected in the vessel wall by immunocytochemistry and in situ hybridization. As an additional control, the effect of adenovirus on cell proliferation was analyzed by performing gene transfer to intact aorta without endothelial denudation. No differences were seen in smooth muscle cell proliferation or I/M between lacZ adenovirus and 0.9% saline-treated animals. CONCLUSIONS: Adenovirus-mediated **VEGF**-C gene transfer may be useful for the treatment of postangioplasty **restenosis** and vessel wall thickening after vascular manipulations.

L9 ANSWER 4 OF 4 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:106500 BIOSIS
TI Clinical applications of angiogenic growth factors and their inhibitors.
SO Nature Medicine, (Dec., 1999) Vol. 5, No. 12, pp. 1359-1364.
ISSN: 1078-8956.
AU Ferrara, Napoleone (1); **Alitalo, Kari (1)**
AB Promoting the formation of new collateral vessels in ischemic tissues

using angiogenic growth factors (therapeutic angiogenesis) is a an exciting frontier of cardiovascular medicine. Conversely, inhibition of the action of key regulators of angiogenesis, such as **VEGF**, constitutes a promising approach for the treatment of solid tumors and intraocular neovascular syndromes. These concepts are being tested now in clinical trials.

=>

(FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, BIOSIS, MEDICONF'
ENTERED AT 14:10:18 ON 15 JUL 2002)
DEL HIS

L1 206845 S RESTENOSIS OR STENOSIS
L2 630 S L1 AND (VEGF? OR (VASCULAR ENDOTHELIAL))
L3 358 DUP REM L2 (272 DUPLICATES REMOVED)
L4 269 S L3 AND (GENE OR DNA OR DEOXY? OR TRANS? OR VIR? OR VECTOR)
L5 269 FOCUS L4 1-

=> d an ti so au ab pi 15 1-9

L5 ANSWER 1 OF 269 CAPLUS COPYRIGHT 2002 ACS
AN 2000:290851 CAPLUS
DN 132:318341
TI Use of **VEGF**-C or **VEGF**-D **gene** or protein to prevent **restenosis**
SO PCT Int. Appl., 61 pp.
CODEN: PIXXD2
IN Yla-Herttuala, Seppo; Alitalo, Kari; Hiltunen, Mikko O.; Jeltsch, Markku M.; Achen, Marc G.
AB The present invention provides materials and methods for preventing **stenosis** or **restenosis** of a blood vessel using **Vascular Endothelial** Growth Factor C (**VEGF**-C) and/or **Vascular Endothelial** Growth Factor D (**VEGF**-D) **genes** or proteins. A medical device designed to contact a surface of a blood vessel in the course of surgery to treat **stenosis** of the blood vessel is also claimed, the device characterized by an improvement comprising integrating into the device a compn. effective to prevent **restenosis**, said compn. comprising at least one anti-**restenosis** agent selected from the group consisting of a **VEGF**-C polynucleotide, a **VEGF**-C polypeptide, a **VEGF**-D polynucleotide, and a **VEGF**-D polypeptide. The medical device is selected from the group consisting of intravascular stents, intravascular catheters, extravascular collars, elastomeric membranes adapted to cover a surface of an intravascular stent or catheter, and combinations thereof. Also claimed is a kit for treating **restenosis** comprising a container holding at least one anti-**restenosis** agent of the invention and a label attached to or packaged with the container, the label describing use of the compd. for prevention of **restenosis** of a blood vessel. The kit further comprises a medical device of the invention.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000024412	A2	20000504	WO 1999-US24054	19991026
WO 2000024412	A3	20000803		
W: AU, CA, CN, JP, NO, NZ				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1126870	A2	20010829	EP 1999-956559	19991026
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NO 2001002017	A	20010626	NO 2001-2017	20010424

L5 ANSWER 2 OF 269 CAPLUS COPYRIGHT 2002 ACS
AN 2002:505921 CAPLUS
TI Increased vascularity detected by digital subtraction angiography after **VEGF gene transfer** to human lower limb artery: a randomized, placebo-controlled, double-blinded phase II study
SO Molecular Therapy (2002), 6(1), 127-133
CODEN: MTOHCK; ISSN: 1525-0016
AU Makinen, Kimmo; Manninen, Hannu; Hedman, Marja; Matsi, Pekka; Mussalo, Hanna; Alhava, Esko; Yla-Herttuala, Seppo
AB **Vascular endothelial** growth factor (**VEGF**) **gene** therapy may be useful for the treatment of lower-limb ischemia. The objectives of this study were to evaluate safety and angiog. and hemodynamic responses of local catheter-mediated **VEGF gene** therapy in ischemic lower-limb arteries after percutaneous **transluminal** angioplasty (PTA). For this study, we recruited patients with chronic lower-limb ischemia and atherosclerotic infrainguinal occlusion or **stenosis** suitable for PTA. In the

study, 18 patients received 2 .times. 1010 plaque-forming units (pfu) **VEGF**-adenovirus (**VEGF**-Ad), 17 patients received **VEGF**-plasmid/liposome (**VEGF**-P/L; 2000 .mu.g of **VEGF** plasmid, 2000 .mu.l of DOTMA:DOPE), and 19 control patients received Ringer's lactate at the angioplasty site. Digital subtraction angiog. (DSA) was used to evaluate vascularity before, immediately after, and 3 mo after the PTA. Clin. follow-up data, basic lab. tests, and ankle-brachial index (ABI) were evaluated. Primary endpoint was DSA anal. of vascularity, and secondary endpoints were **restenosis** rate, Rutherford class, and ABI after 3 mo follow-up. No major **gene** **transfer**-related side effects or differences in lab. tests were detected between the study groups. However, anti-adenovirus antibodies increased in 61% of the patients treated with **VEGF**-Ad. For the primary endpoint, follow-up DSA revealed increased vascularity in the **VEGF**-treated groups distally to the **gene** **transfer** site (**VEGF**-Ad P = 0.03, **VEGF**-P/L P = 0.02) and in the **VEGF**-Ad group in the region of the clin. most severe ischemia (P = 0.01). As for the secondary endpoints, mean Rutherford class and ABI showed statistically significant improvements in the **VEGF**-Ad and **VEGF**-P/L groups, but similar improvements were also seen in the control patients. We conclude that catheter-mediated **VEGF gene** therapy is safe and well tolerated. Angiog. demonstrated that **VEGF gene** **transfer** increased vascularity after PTA in both **VEGF** -Ad- and **VEGF**-P/L-treated groups.

L5 ANSWER 3 OF 269 CAPLUS COPYRIGHT 2002 ACS
AN 2000:35393 CAPLUS
DN 132:176176
TI Effect of liposome-mediated **vascular endothelial** growth factor **gene** on proliferation of cultured vascular cells
SO Zhongguo Bingli Shengli Zazhi (1999), 15(10), 874-876
CODEN: ZBSZEB; ISSN: 1000-4718
AU Jiang, Xue-Jun; Wei, Wei; Xiong, Yi-Li; Lu, Zai-Ying
AB The aim of the study was to observe the expression of liposome-mediated **vascular endothelial** growth factor (**VEGF**) **gene** of in vitro vascular smooth muscle cells (VSMC), and compare the effect of **VEGF** on proliferation of vessel endothelium cell and VSMC. An eukaryotic expression **vector** pSVI21 contg. **VEGF** cDNA was **transferred** into VSMC in vitro by lipofectamine reagent-mediated method. **Vascular** **endothelial** cells (VEC) were cultured with the above VSMC conditioned medium. In order to det. the expression of **VEGF** mRNA in VSMC and **VEGF** antigen in VSMC conditional medium, and to compare the effect of **VEGF** on proliferation of VEC and VSMC, Northern blot, Western blot and [3H]-thymidine ([3H]TdR) incorporation were used. The expression of **VEGF** mRNA in **transgene** VSMC groups was higher. The expression of **VEGF** antigen in **transgenic** medium was significantly higher (P < 0.01) than control group, [3H]TdR data(counts-min-1) was significantly higher in VEC groups added **transgenic** medium than control group (P < 0.01),but there was no significant difference between VSMC groups. The method of liposome-mediated **VEGF gene transfer** into VSMC is successful. **VEGF** might promote proliferation of VEC, but did not cause proliferation of VSMC, which is favorable for preventing and treating ischemic disease and artery **restenosis**.

L5 ANSWER 4 OF 269 CAPLUS COPYRIGHT 2002 ACS
AN 2001:535146 CAPLUS
DN 136:303773
TI **Gene** therapy with human **vascular endothelial** growth factor in prevention of **restenosis** after angioplasty
SO Dier Junyi Daxue Xuebao (2001), 22(5), 443-446
CODEN: DJXUE5; ISSN: 0258-879X
AU Chen, Shaoping; Gu, Hong; Wang, Yongchun; Win, Yongwen; Zhang, Guoyuan
AB The effect of human **vascular endothelial** growth factor on **restenosis** after angioplasty was studied. A rabbit model of injured carotid artery was made by percutaneous **transluminal** angioplasty. The pcDNA3/hVEGF165 (500 .mu.g, n = 12) and pcDNA3(500 .mu.g, n = 12) were **transfected** into injured arterial wall

cultured for 30 min, resp. The carotid artery was imaged by aortic angiog. at the 2nd week and 4th week and obsd. by pathol. anal. and Northern blot anal. Aortic angiog. showed that carotid artery diam. narrowness was obviously lessened at the 2nd week and 4th week in the exptl. group more than that in control group. H-E stains showed lumina narrow ratio was obviously reduced at the 2nd week and 4th week in the exptl. group more than that in control group [(9.58 .+-. 1.35)% vs. (31.72 .+-. 1.72)%; (18.09 .+-. 2.93)% vs. %, P <0.01]. Northern blot anal. showed that the expression of hVEGF165 mRNA in the exptl. group was up-regulated as compared with the control group. The results showed that smooth muscle cell **transfected** with pcDNA3/hVEGF165 can secrete bioactive protein after >4 wk of **transfection** and can accelerate re-endothelialization and prevent **restenosis**.

L5 ANSWER 5 OF 269 CAPLUS COPYRIGHT 2002 ACS
AN 2000:456818 CAPLUS
DN 133:53712
TI Efficient and stable in vivo **gene transfer** to cardiomyocytes using recombinant adeno-associated **virus vectors**
SO PCT Int. Appl., 20 pp.
CODEN: PIXXD2
IN Leiden, Jeffrey M.; Svensson, Eric
AB Recombinant adeno-assocd. **virus** (rAAV) **vectors** are used to **transduce** cardiomyocytes in vivo by infusing the rAAV into a coronary artery or coronary sinus. RAAV infection is not assocd. with detectable myocardial inflammation or myocyte necrosis. Thus, rAAV is a useful **vector** for the stable expression of therapeutic **genes** in the myocardium and can be used to deliver **genes** for inducing angiogenesis, inhibiting angiogenesis, stimulating cell proliferation, inhibiting cell proliferation and/or treating or ameliorating other cardiovascular conditions.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000038518	A1	20000706	WO 1999-US31093	19991228
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1139751	A1	20011010	EP 1999-967703	19991228
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

L5 ANSWER 6 OF 269 CAPLUS COPYRIGHT 2002 ACS
AN 2001:165733 CAPLUS
DN 134:202698
TI Expression **vectors** for **genes** for angiogenic factors and **restenosis** inhibitors for use in the therapy of peripheral arterial occlusive disease in diabetes mellitus
SO Ger. Offen., 16 pp.
CODEN: GWXXBX
IN Faerber, Karin; Roesen, Peter; Tschoepe, Diethelm
AB Expression **vectors** contg. **genes** for angiogenic factors and inhibitors of **restenosis** that can be used to treat peripheral arterial occlusive disease that is a complication of diabetes mellitus are described. The preferred angiogenic factor is the 165-amino acid isoform of **vascular endothelial** growth factor (**VEGF165**) and the **restenosis** inhibitor may be selected from constitutive nitric oxide synthase, prostacyclin synthase, leptin or thrombomodulin. The **genes** may be present on sep. **vectors** or on a dicistronic expression **vector**.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE 19940012	A1	20010308	DE 1999-19940012	19990824

L5 ANSWER 7 OF 269 CAPLUS COPYRIGHT 2002 ACS
AN 2000:841957 CAPLUS
DN 133:366470
TI Methods and compositions for non-**viral gene** therapy for treatment of hyperproliferative diseases
SO PCT Int. Appl., 148 pp.
CODEN: PIXXD2
IN Ramesh, Rajagopal; Roth, Jack A.; Saeki, Tomoyuki; Wilson, Deborah
AB The present invention relates to non-**viral gene** therapy methods and compns. for treatment of hyperproliferative disease in humans. More specifically, the invention is directed, in one embodiment, to lipid formulations which form stable liposome structures, capable of efficient in vivo nucleic acid **transfer**. In other embodiments, methods and compns. are directed to liposome **transfer** of anti-proliferative nucleic acids, wherein the **transfer** of the nucleic acids is cell specific via cell specific targeting moieties. The present invention thus provides non-**viral**, liposome compns. and methods of **gene transfer** particularly useful for targeting and treating hyperproliferative disease.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000071096	A2	20001130	WO 2000-US14350	20000524
WO 2000071096	A3	20010503		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1180016	A2	20020220	EP 2000-936279	20000524

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, PT, IE, SI, LT, LV, FI, RO

L5 ANSWER 8 OF 269 CAPLUS COPYRIGHT 2002 ACS
AN 2000:21797 CAPLUS
DN 132:73132
TI **Gene** therapy for cardiovascular diseases
SO Saishin Igaku (2000), 55(1), 38-43
CODEN: SAIGAK; ISSN: 0370-8241
AU Aoki, Motokuni; Morishita, Ryuichi; Kaneda, Yasufumi
AB A review with 7 refs., on the strategies for **gene** therapy of **restenosis** following PTCA or PTA, and **gene** therapy for myocardial angiogenesis. Topics discussed include: suppression of vascular smooth muscle cell proliferation by **gene** therapy, remodeling improvement of **restenosis** by **VEGF** or HGF **gene transfer**, and **gene** therapy for arteriosclerosis obliterans and angina pectoris with **VEGF** or HGF **gene**.

L5 ANSWER 9 OF 269 CAPLUS COPYRIGHT 2002 ACS
AN 1998:176020 CAPLUS
DN 128:239477
TI **Vascular endothelial** growth factor isoform **VEGF145** as an angiogenic factor in treating cardiovascular disease
SO PCT Int. Appl., 73 pp.
CODEN: PIXXD2
IN Neufeld, Gera; Keshet, Eli; Vlodavsky, Israel; Poltorak, Zoya
AB The present invention relates to a novel **VEGF** protein product, and nucleic acid encoding the novel protein product, comprising exons 1-6 and 8 of the **VEGF gene**, and its use in treating the cardiovascular system and its diseases through effects on anatomy, conduit function, and permeability. **VEGF145** is an active mitogen for **vascular endothelial** cells and functions as an angiogenic factor in vivo. **VEGF145** has novel properties compared with previously characterized **VEGF** species with respect to cellular distribution, susceptibility to oxidative damage, and extracellular matrix (ECM) binding ability. The present invention

provides methods of treating the cardiovascular system, enhancing endothelialization of diseased vessels, and enhancing drug permeation by providing the novel **VEGF** protein product. The invention also provides expression **vectors**, compns., and kits for use in the methods of the invention.

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9810071	A1	19980312	WO 1997-US15471	19970904
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 6013780	A	20000111	US 1997-784551	19970121
	AU 9742471	A1	19980326	AU 1997-42471	19970904
	AU 737898	B2	20010906		
	EP 925360	A1	19990630	EP 1997-940771	19970904
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	CN 1236390	A	19991124	CN 1997-199495	19970904
	JP 2001500728	T2	20010123	JP 1998-512834	19970904

=>

```
 (FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, BIOSIS, MEDICONF'
     ENTERED AT 14:10:18 ON 15 JUL 2002)
                DEL HIS
L1       206845 S RESTENOSIS OR STENOSIS
L2          630 S L1 AND (VEGF? OR (VASCULAR ENDOTHELIAL))
L3          358 DUP REM L2 (272 DUPLICATES REMOVED)
L4          269 S L3 AND (GENE OR DNA OR DEOXY? OR TRANS? OR VIR? OR VECTOR)
L5          269 FOCUS L4 1-
L6           96 S L5 AND PY<=1998
L7            1 S L6 AND (VEGF-D OR VEGF-C)

=> d l7 1 all

L7   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2002 ACS
AN   2002:444386  CAPLUS
DN   137:19390
TI   VEGF-C polypeptides, polynucleotides and anti-
     VEGF-C antibodies for diagnosing and treating
     endothelial or angiogenic diseases
IN   Alitalo, Kari; Joukov, Vladimir
PA   Helsinki University Licensing, Ltd., Finland; Ludwig Institute for Cancer
     Research
SO   U.S., 71 pp., Cont.-in-part of U.S. 6,245,530.
     CODEN: USXXAM
DT   Patent
LA   English
IC   ICM  A61K039-395
     ICS  C07K016-22
NCL  424139100
CC   15-3 (Immunochemistry)
     Section cross-reference(s): 1, 2, 3, 8, 9, 63
FAN.CNT 9
     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
PI   US 6403088         B1   20020611       US 1996-601132   19960214
     US 6221839         B1   20010424       US 1995-510133   19950801
     US 6245530         B1   20010612       US 1996-585895   19960112
     CA 2228248         AA   19970213       CA 1996-2228248  19960801 <--
     WO 9705250         A2   19970213       WO 1996-FI427    19960801 <--
     WO 9705250         A3   19970410
         W:  AU, CA, CN, JP, NO, NZ, US
         RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
     AU 9666169         A1   19970226       AU 1996-66169    19960801 <--
     AU 711578          B2   19991014
     EP 842273          A2   19980520       EP 1996-925768   19960801 <--
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
     JP 11510689        T2   19990921       JP 1996-507262   19960801
     WO 9833917         A1   19980806       WO 1998-US1973   19980202 <--
         W:  AU, CA, CN, JP, NZ, US, US, US, US, US, US, US
         RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
PRAI US 1995-510133    A2   19950801
     US 1996-585895    A2   19960112
     US 1994-340011    A2   19941114
     US 1996-601132    A    19960214
     US 1996-671573    A    19960628
     WO 1996-FI427     W    19960801
     US 1997-795430    A2   19970205
AB   The invention discloses VEGF-C, a polypeptide ligand
     for Flt4 receptor tyrosine kinase (VEGFR-3), polynucleotides
     encoding them, and antisense oligonucleotides for diagnosis, therapy and
     drug screening use.  The invention also provides monoclonal and polyclonal
     antibodies that are reactive with VEGF-C for
     diagnostic application to monitor angiogenesis, vascularization, lymphatic
     vessels and their disease states, wound healing, or certain hematopoietic
     or leukemia cells, and for blockade or activation of Flt4 receptor.  The
     ligand and antibody may be coupled to supermagnetic , paramagnetic,
     electron dense, echogenic, or radioactive agent for imaging.
ST   VEGFC VEGFR3 Flt4 receptor ligand angiogenesis disease
IT   Animal cell line
```

Culture media
DNA sequences
Drug screening
Eye, disease
Genetic mapping
Genetic **vectors**
Hypoxia, animal
Imaging
Imaging agents
Labels
Leukemia
Molecular cloning
Paramagnetic materials
Protein sequences
Transplant and **Transplantation**
Wound healing
(**VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT Antibodies
RL: BPN (Biosynthetic preparation); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT Antisense oligonucleotides
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT Avidins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT Polynucleotides
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT Radionuclides, biological studies
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT cDNA
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT Human
Mouse
(**VEGF-C**; **VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT **Gene**, animal
Proteins
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**VEGF-C**; **VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT Ligands
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);

DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**VEGFR3**; **VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT Immunostimulants
(adjuvants; **VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT Phosphorylation, biological
(autophosphorylation, **VEGFR**-2; **VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT Drug delivery systems
(carriers; **VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT Blood vessel
(collateral, formation; **VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT Lymphatic system
(disease, obstruction and lymphangioma; **VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT Hematopoiesis
(disorders; **VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT Infection
(elephantiasis; **VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT Cell migration
(endothelial cells; **VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT **Vascular endothelial** growth factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**gene** KDR, autophosphorylation; **VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT **Vascular endothelial** growth factor receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**gene** flt 4, ligand; **VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT Disease, animal
(genetic, Milroy's disease; **VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT Chromosome
(human 4, 4q34; **VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT Diagnosis
(immunodiagnosis; **VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT Chemotaxis
(leukocytes; **VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT Lymphatic system
(lymph vessel, diseases; **VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT Edema
Inflammation
(lymphatic vessel; **VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT Antibodies
RL: BPN (Biosynthetic preparation); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(monoclonal; **VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT Plasmids
(pFLT4-L; **VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT Proteins
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(precursor, **VEGF-C**; **VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT Angiogenesis inhibitors
(screening; **VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT Artery, disease
(**stenosis**; **VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT Magnetic materials
(super-; **VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT Leukocyte
(trafficking; **VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT Vein
(venule, endothelium, disease; **VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT 300766-50-1P 435233-56-0P 435233-57-1P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT 384497-77-2P, GenBank X68203 386563-31-1P, GenBank S66407
392214-95-8P, GenBank X60280
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation)
(**VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT 58-85-5, Biotin
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT 127464-60-2, **Vascular endothelial** growth factor
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**VEGF-C**; **VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT 435233-74-2P 435233-76-4P

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; **VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT 144638-77-7, FLT4 receptor tyrosine kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ligand; **VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT 435233-75-3P 435233-77-5P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nucleotide sequence; **VEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT 435236-81-0 435236-82-1 435236-83-2 435236-84-3 435236-85-4
435236-86-5 435236-87-6 435236-88-7 435236-89-8 435236-90-1
435236-92-3 435236-93-4 435236-94-5 435236-95-6 435236-96-7
435236-97-8 435236-98-9 435236-99-0 435237-00-6 435237-01-7
435237-02-8 435237-03-9 435237-04-0 435237-05-1
RL: PRP (Properties)
(unclaimed nucleotide sequence; **vEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT 435237-06-2 435237-07-3 435237-08-4 435237-09-5 435237-10-8
RL: PRP (Properties)
(unclaimed protein sequence; **vEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

IT 335591-30-5 335591-31-6 335591-32-7 335591-33-8 435236-91-2
RL: PRP (Properties)
(unclaimed sequence; **vEGF-C** polypeptides, polynucleotides and anti-**VEGF-C** antibodies for diagnosing and treating endothelial or angiogenic diseases)

RE.CNT 188 THERE ARE 188 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Achen, M; Proceedings of the National Academy of Science, USA 1998, V95, P548 CAPLUS
(2) Adams, M; GenBank Accession No AA298182 1997
(3) Adams, M; GenBank Accession No AA298283 1997
(4) Adams, M; Nature 1995, V377(6547 Supplement), P3
(5) Alitalo; 2nd Symposium on Current Problems in Molecular Medicine:The Role of Cytokines in Human Disease 1996, P1
(6) Alitalo; The 9th International Conference of the International Society of Differentiation (ISD), Development, Cell Differentiation and Cancer, Abstract S22 1996, P66
(7) Anderson; J Biol Chem 1992, V267(16), P11260
(8) Andersson; US 5326695 A 1994 CAPLUS
(9) Anon; EP 0506477 A1 1992 CAPLUS
(10) Anon; WO 9524473 A1 1995 CAPLUS
(11) Anon; WO 9533050 1995 CAPLUS
(12) Anon; WO 9533772 1995 CAPLUS
(13) Anon; WO 9611269 A2 1996 CAPLUS
(14) Anon; WO 9630046 1996 CAPLUS
(15) Anon; WO 9639421 1996 CAPLUS
(16) Anon; WO 9639515 1996 CAPLUS
(17) Anon; WO 9705250 A 1997 CAPLUS
(18) Anon; WO 9709427 A 1997 CAPLUS
(19) Anon; WO 9717442 A 1997 CAPLUS
(20) Anon; GenBank Accession No Z40230 1995
(21) Anon; GenBank Accession No Z44272 1995
(22) Aprelikova; Cancer Research 1992, V52, P746 CAPLUS
(23) Aprelikova, O; GenBank Accession No X68203 1993
(24) Ausprunk; Microvasc Res 1977, V14, P53 MEDLINE
(25) Basilico; Adv Cancer Res 1992, V59, P145
(26) Berse; Mol Biol Cell 1992, V3, P211 CAPLUS

(27) Betsholtz; Nature 1986, V320, P695 CAPLUS
(28) Borg; Oncogene 1995, V10, P973 CAPLUS
(29) Bowie; Science 1990, V247, P1306 CAPLUS
(30) Breier; Development 1992, V114, P521 CAPLUS
(31) Cao; J Biol Chem 1996, V271(6), P3154 CAPLUS
(32) Cheng; Cell 1994, V79, P157 CAPLUS
(33) Claesson-Welsh; J Biol Chem 1989, V264(3), P1742 CAPLUS
(34) Claesson-Welsh; Mol Cell Biol 1988, V8(8), P3476 CAPLUS
(35) Claesson-Welsh; Proc Nat'l Acad Sci USA 1989, V86(13), P4917 CAPLUS
(36) Coffin; Devel Biol 1991, V148, P51 MEDLINE
(37) Cohen, T; Journal of Biological Chemistry 1995, V270(19), P11322 CAPLUS
(38) Collins; GenBank Accession No X02811 1995
(39) Collins; Nature 1985, V316, P748 CAPLUS
(40) Curran; Cell 1988, V55, P395 CAPLUS
(41) Dame, J; GenBank Accession No AA549856 1997
(42) de Vries; Science 1992, V255, P989 CAPLUS
(43) Dignam; Gene 1990, V88, P133 CAPLUS
(44) Disalvo; J Biol Chem 1995, V270(13), P7717 CAPLUS
(45) Don; Nucl Acids Res 1991, V19, P4008 CAPLUS
(46) Dressler; Handbook of Experimental Immunology in Four Volumes 1986, P8.1
(47) Dumont; Development Dynamics 1995, V203, P80 CAPLUS
(48) Dumont; Genes Dev 1994, V8, P1897 CAPLUS
(49) Dvorak; Amer J Path 1995, V146, P1029 CAPLUS
(50) Eichmann; Mech Dev 1993, V42, P33 CAPLUS
(51) Eriksson; US 5607918 A 1997 CAPLUS
(52) Ferrara; US 5332671 A 1994 CAPLUS
(53) Ferrara; Endocrine Rev 1992, V13(1), P18 CAPLUS
(54) Finnerty; Oncogene 1993, V8(11), P2293
(55) Flamme; Devel Biol 1995, V169, P699 CAPLUS
(56) Flanagan; Cell 1990, V63, P185 CAPLUS
(57) Folkman; J Biol Chem 1992, V267(16), P10931 CAPLUS
(58) Folkman; Nature Med 1995, V1(1), P27 CAPLUS
(59) Folkman; Proc Nat'l Acad Sci, USA 1979, V76(10), P5217 MEDLINE
(60) Fong; Nature 1995, V376, P66 CAPLUS
(61) Fossum; J Vet Int Med 1992, V6, P283 MEDLINE
(62) Fournier; Oncogene 1995, V11(5), P921 CAPLUS
(63) Friesel; FASEB J 1995, V9, P919 CAPLUS
(64) Galland; Oncogene 1993, V8, P1233 CAPLUS
(65) Harlow; Antibodies, A Laboratory Manual 1988, P72 MEDLINE
(66) Hehl, A; GenBank Accession No N82975 1997
(67) Heldin; Growth Factors 1993, V8, P245 MEDLINE
(68) Hillier, L; GenBank Accession No AA149461 1997
(69) Hillier, L; GenBank Accession No AA406492 1997
(70) Hillier, L; GenBank Accession No AA421713 1997
(71) Hillier, L; GenBank Accession No AA425303 1997
(72) Hillier, L; GenBank Accession No AA425486 1997
(73) Hillier, L; GenBank Accession No AA425486 1997
(74) Hillier, L; GenBank Accession No AA478766 1997
(75) Hillier, L; GenBank Accession No AA479987 1997
(76) Hillier, L; GenBank Accession No H05134 1995
(77) Hillier, L; GenBank Accession No H07899 1995
(78) Hillier, L; GenBank Accession No H81867 1995
(79) Hillier, L; GenBank Accession No H81868 1995
(80) Hillier, L; GenBank Accession No H96533 1996
(81) Hillier, L; GenBank Accession No H96876 1996
(82) Hillier, L; GenBank Accession No II05177 1995
(83) Hillier, L; GenBank Accession No N31713 1996
(84) Hillier, L; GenBank Accession No N31720 1996
(85) Hillier, L; GenBank Accession No N42368 1996
(86) Hillier, L; GenBank Accession No N42374 1996
(87) Hillier, L; GenBank Accession No N50972 1996
(88) Hillier, L; GenBank Accession No N94399 1996
(89) Hillier, L; GenBank Accession No R77495 1995
(90) Hillier, L; GenBank Accession No T81481 1995
(91) Hillier, L; GenBank Accession No T84377 1995
(92) Hillier, L; GenBank Accession No T89295 1995
(93) Hillier, L; GenBank Accession NoT81690 1995
(94) Hu; US 5932540 A 1999 CAPLUS
(95) Hu; US 5935820 A 1999 CAPLUS
(96) Jeltsch, M; Science 1997, V276, P1423 CAPLUS

(97) Joukov; EMBO J 1996, V15, P290 CAPLUS
(98) Joukov; EMBO J 1996, V15(2), P290 CAPLUS
(99) Joukov; GenBank Accession No X94216 1996
(100) Joukov, V; EMBO Journal 1997, V16(13), P3898 CAPLUS
(101) Joukov, V; Journal of Biological Chemistry 1998, V273(12), P6599 CAPLUS
(102) Kainpainen; Cancer Res 1994, V54, P6571
(103) Kaipainen; J Exp Med 1993, V178, P2077 CAPLUS
(104) Kaipainen; Proc Nat'l Acad Sci, USA 1995, V92, P3566 CAPLUS
(105) Keck; GenBank Accession No X15997 1990
(106) Keyt; J Biol Chem 1996, V271(10), P5638 CAPLUS
(107) Kim; Growth Factors 1992, V7, P53 MEDLINE
(108) Kozak; Nucl Acids Res 1987, V15, P8125 CAPLUS
(109) Kukk; Development 1996, V122, P3829 CAPLUS
(110) Kukk; Development 1996, V122, P3829 CAPLUS
(111) Lee; Proc Nat'l Acad Sci, USA 1996, V93, P1988 CAPLUS
(112) Leung; Science 1989, V246, P1306 CAPLUS
(113) Levy; J Biol Chem 1995, V270(22), P13333 CAPLUS
(114) Levy; J Biol Chem 1996, V271(5), P2746 CAPLUS
(115) Lyman; Cell 1993, V75, P1157 CAPLUS
(116) Maekelae, T; GenBank Accession No X60280 1996
(117) Maglione; Oncogene 1993, V8, P925 CAPLUS
(118) Maglione; Proc Nat'l Acad Sci, USA 1991, V88, P9267 CAPLUS
(119) Makela; Gene 1992, V118, P293 CAPLUS
(120) Marra, M; GenBank Accession No AA285997 1997
(121) Matthews; Proc Nat'l Acad Sci, USA 1991, V88, P9026 CAPLUS
(122) Metzelaar; J of Biol Chem 1991, V266(5), P3239 CAPLUS
(123) Millauer; Cell 1993, V72, P835 CAPLUS
(124) Millauer; Nature 1994, V367, P576 CAPLUS
(125) Mitchell; Genes and Dev 1991, V5, P105 CAPLUS
(126) Morgenstern; Nucl Acids Res 1990, V18(12), P3587 CAPLUS
(127) Mount, S; Nucl Acids Res 1982, V10(2), P459 CAPLUS
(128) Mustonen; J Cell Biol 1995, V129, P895 CAPLUS
(129) Nelson; J Cell Biol 1983, V97, P244 CAPLUS
(130) Neufeld; Prog Growth Fact Res 1994, V5, P89 CAPLUS
(131) Oefner; EMBO J 1992, V11(11), P3921 CAPLUS
(132) Oelrichs; Oncogene 1993, V8, P11 CAPLUS
(133) Okubo, K; GenBank Accession No C21512 1996
(134) Olofsson; GenBank Accession No U48800 1996
(135) Olofsson; GenBank Accession No U48801 1996
(136) Olofsson; Proc Nat'l Acad Sci, USA 1996, V93, P2576 CAPLUS
(137) Paavonen; Circulation 1996, V93(6), P1079 CAPLUS
(138) Paavonen; IX International Vascular Biology Meeting, Abstract 229 1996, P76
(139) Pajosola; Cancer Res 1992, V52, P5738
(140) Pajosola; Oncogene 1993, V8, P2931
(141) Pajosola; Oncogene 1994, V9, P3545
(142) Pajusola; Academic Dissertation, Molecular/Cancer Biology Laboratory and Department of Pathology, Haartman Institute and Department of Biosciences, Division of Genetics, University of Helsinki 1996
(143) Pajusola; GenBank Accession No S66407 1993
(144) Park; J Biol Chem 1994, V269(41), P25646 CAPLUS
(145) Partanen; Mol & Cell Biol 1992, V12(4), P1698 CAPLUS
(146) Partanen; Proc Nat'l Acad Sci, USA 1990, V87, P8913 CAPLUS
(147) Paulsson; J Mol Biol 1990, V211, P331 CAPLUS
(148) Pear; Proc Nat'l Acad Sci USA 1993, V90, P8392 CAPLUS
(149) Persico, M; GenBank Accession No X54936 1991
(150) Pertovaara; J Biol Chem 1994, V269(9), P6271 CAPLUS
(151) Peters; Proc Nat'l Acad Sci, USA 1993, V90, P8915 CAPLUS
(152) Potgens; J Biol Chem 1994, V269(52), P32879 MEDLINE
(153) Puri; EMBO J 1995, V14, P5884 CAPLUS
(154) Quinn; Proc Nat'l Acad Sci USA 1993, V90, P7533 CAPLUS
(155) Risau; Devel Biol 1988, V125, P441 CAPLUS
(156) Risau; Growth Factors 1992, V7, P261 MEDLINE
(157) Risau, W; FASEB J 1995, V9, P926 CAPLUS
(158) Sabin, F; Am J Anat 1909, V9(1), P43
(159) Saksela; Ann Rev Cell Biol 1988, V4, P93 CAPLUS
(160) Sambrook; Molecular Cloning, a Laboratory Manual, Second Edition 1989, P2.60
(161) Sato; Nature 1995, V376, P70 CAPLUS
(162) Schmeltz; Differentiation 1994, V57, P97

(163) Schneider; J Biol Chem 1982, V257(18), P10766 CAPLUS
(164) Seetharam; Oncogene 1995, V10, P135 CAPLUS
(165) Senger; Science 1983, V219, P983 MEDLINE
(166) Shalaby; Nature 1995, V376, P62 CAPLUS
(167) Shibuya; Oncogene 1990, V5, P519 CAPLUS
(168) Shibuya, M; Adv Cancer Res 1995, V67, P281 CAPLUS
(169) Shweiki; J Clin Invest 1993, V91, P2235 CAPLUS
(170) Sitaras; Cancer Research 1988, V48(7), P1930 CAPLUS
(171) Southern; J Mol Appl Genet 1982, V1, P327 CAPLUS
(172) Terman; Biochem Biophys Res Commun 1992, V187, P1579 CAPLUS
(173) Terman; Growth Factors 1994, V11(3), P187 MEDLINE
(174) Terman; Oncogene 1991, V6, P1677 CAPLUS
(175) Tessier; Gene 1991, V98, P177 CAPLUS
(176) Tischer; J Biol Chem 1991, V266(18), P11947 CAPLUS
(177) Tisher; US 5219739 A 1993 CAPLUS
(178) van der Geer; Ann Rev Cell Biol 1994, V10, P251 CAPLUS
(179) Vassar; Genes & Dev 1991, V5, P714 CAPLUS
(180) Vassar; Proc Nat'l Acad, Sci, USA 1989, V86, P1563 CAPLUS
(181) Vassbotn; Mol Cell Biol 1993, V13(7), P4066 CAPLUS
(182) Vastrik; J Cell Biol 1995, V128(6), P1197 CAPLUS
(183) Von Heijne, G; Nucleic Acids Res 1986, V14(11), P4683 CAPLUS
(184) Waltenberger; J Biol Chem 1994, V269(43), P26988 CAPLUS
(185) Wanaka; Development 1991, V111, P455 MEDLINE
(186) Wells; Biochemistry 1990, V29(37), P8509 CAPLUS
(187) Wen; Cell 1992, V69, P559 CAPLUS
(188) Yamane; Oncogene 1994, V9, P2683 CAPLUS

=>

(FILE 'HOME' ENTERED AT 14:10:09 ON 15 JUL 2002)

FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, BIOSIS, MEDICONF'
ENTERED AT 14:10:18 ON 15 JUL 2002
E RESTONOSIS
L1 19 S E3
E STENOSIS
L2 183734 S E3
L3 183748 S RESTONOSIS OR STENOSIS
L4 86 S L3 AND VEGF?
L5 55 DUP REM L4 (31 DUPLICATES REMOVED)
L6 55 FOCUS L5 1-
L7 34 S L5 AND (GENE OR DNA OR DEOXY? OR TRANS? OR VIR? OR VECTOR)
E ALITALO KAR?/AU
L8 543 S E5
L9 5 S L8 AND L3
L10 4 DUP REM L9 (1 DUPLICATE REMOVED)
L11 209 S L3 AND (GENE THERAP?)
L12 135 DUP REM L11 (74 DUPLICATES REMOVED)
L13 16 S L12 AND (VEGF? OR (VASCULAR ENDOTHELIAL))

=> d an ti so au ab pi l13 11 2 4 6 9 10 13

L13 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2002 ACS
AN 2000:290851 CAPLUS
DN 132:318341
TI Use of **VEGF**-C or **VEGF**-D gene or protein to prevent restenosis
SO PCT Int. Appl., 61 pp.
CODEN: PIXXD2
IN Yla-Herttuala, Seppo; Alitalo, Kari; Hiltunen, Mikko O.; Jeltsch, Markku M.; Achen, Marc G.
AB The present invention provides materials and methods for preventing **stenosis** or restenosis of a blood vessel using **Vascular Endothelial** Growth Factor C (**VEGF**-C) and/or **Vascular Endothelial** Growth Factor D (**VEGF**-D) genes or proteins. A medical device designed to contact a surface of a blood vessel in the course of surgery to treat **stenosis** of the blood vessel is also claimed, the device characterized by an improvement comprising integrating into the device a compn. effective to prevent restenosis, said compn. comprising at least one anti-restenosis agent selected from the group consisting of a **VEGF**-C polynucleotide, a **VEGF**-C polypeptide, a **VEGF**-D polynucleotide, and a **VEGF**-D polypeptide. The medical device is selected from the group consisting of intravascular stents, intravascular catheters, extravascular collars, elastomeric membranes adapted to cover a surface of an intravascular stent or catheter, and combinations thereof. Also claimed is a kit for treating restenosis comprising a container holding at least one anti-restenosis agent of the invention and a label attached to or packaged with the container, the label describing use of the compd. for prevention of restenosis of a blood vessel. The kit further comprises a medical device of the invention.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000024412	A2	20000504	WO 1999-US24054	19991026
WO 2000024412	A3	20000803		
W: AU, CA, CN, JP, NO, NZ				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1126870	A2	20010829	EP 1999-956559	19991026
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NO 2001002017	A	20010626	NO 2001-2017	20010424

L13 ANSWER 2 OF 16 MEDLINE
AN 2002046300 MEDLINE
TI Simultaneous surgical revascularization and angiogenic **gene therapy** in diffuse coronary artery disease.
SO EUROPEAN JOURNAL OF CARDIO-THORACIC SURGERY, (2001 Dec) 20 (6) 1128-34.

Journal code: 8804069. ISSN: 1010-7940.

AU Huwer H; Welter C; Ozbek C; Seifert M; Straub U; Greilach P; Kalweit G; Isringhaus H

AB OBJECTIVE: The cytokine **vascular endothelial** growth factor (**VEGF**) is capable of triggering angiogenesis and at higher concentrations vasculogenesis. We report on a pilot study where **VEGF**-DNA as an additional therapy to coronary artery bypass grafting was injected into the myocardium in 24 patients (pts) with proximal coronary artery **stenosis** and diffuse peripheral disease. One region of the myocardium with proven ischemia remained unsupplied after surgery because the respective epicardial coronary artery was not graftable. METHODS AND RESULTS: Plasmid DNA encoding for the 165- and 167-amino acid isoform of the human **VEGF** genes was injected directly into the myocardium, not amenable to surgical revascularization at a dosage of 1000 microg each, using a standardized protocol. A (99m)Tc-sestamibi-SPECT at rest performed 7 days prior to the operation, had shown decreased marker activity in the region of interest. Controls were made 1 week and 80-100 days postoperatively. Transmural scarring was ruled out intraoperatively. Coronary and left ventricular angiographies were performed preoperatively and 3 months postsurgery, respectively. One or more of the following angiographic items were found in 16/24 patients postoperatively. (1) Improvement of regional left ventricular function at the **VEGF** treated myocardial sector (5/24 pts). (2) Newly visible vessels considered as collaterals (8/24 pts). (3) Earlier filling of parent vessels (6/24 pts). (4) An increase in diameter of preoperatively existing collateral vessels (7/24). An increased perfusion at rest in the region of gene application was detected in 3/24 patients by early postoperative (99m)Tc-sestamibi-SPECT investigation. In six additional cases, local perfusion increased markedly until the late examination. No perioperative myocardial infarctions and no signs of inflammation were observed. Newly developed abnormal vasculature was not detected in any patient. CONCLUSIONS: Direct intramyocardial administration of **VEGF**(165)-DNA and **VEGF**(167)-DNA may result occasionally in an enhancement of collateral vascularization in regions with diffuse peripheral coronary artery disease not surgically amenable. During midterm follow-up no adverse effects of **VEGF**-DNA application are observed so far. The very slight midterm improvements caused us to stop further **VEGF**-DNA application and, in our opinion, do not justify a prospective, and randomized study with a control group.

L13 ANSWER 4 OF 16 MEDLINE

AN 2000143033 MEDLINE

TI Catheter-mediated **vascular endothelial** growth factor gene transfer to human coronary arteries after angioplasty.

SO HUMAN GENE THERAPY, (2000 Jan 20) 11 (2) 263-70.
Journal code: 9008950. ISSN: 1043-0342.

AU Laitinen M; Hartikainen J; Hiltunen M O; Eranen J; Kiviniemi M; Narvanen O; Makinen K; Manninen H; Syvanne M; Martin J F; Laakso M; Yla-Herttuala S

AB Blood vessels are among the easiest targets for **gene therapy**. However, no data are available about the safety and feasibility of intracoronary gene transfer in humans. We studied the safety and efficacy of catheter-mediated **vascular endothelial** growth factor (**VEGF**) plasmid/liposome (P/L) gene transfer in human coronary arteries after percutaneous translumenal coronary angioplasty (PTCA) in a randomized, double-blinded, placebo-controlled study. The optimized angioplasty/gene delivery method was previously shown to lead to detectable **VEGF** gene expression in human peripheral arteries as analyzed from amputated leg samples. Gene transfer to coronary arteries was done with a perfusion-infusion catheter, using 1000 microg of **VEGF** or beta-galactosidase plasmid complexed with 1000 microl of DOTMA:DOPE liposomes. Ten patients received **VEGF** P/L, three patients received beta-galactosidase P/L, and two patients received Ringer lactate. Gene transfer to coronary arteries was feasible and well tolerated. Except for a slight increase in serum C-reative protein in all study groups, no adverse effects or abnormalities in laboratory parameters were detected. No **VEGF** plasmid or recombinant **VEGF** protein was present in the systemic circulation after the gene transfer. In control angiography 6 months later, no differences were detected in the degree of coronary **stenosis** between treatment and control groups. We conclude that catheter-mediated

intracoronary gene transfer performed after angioplasty is safe and well tolerated and potentially applicable for the prevention of restenosis and myocardial ischemia.

L13 ANSWER 6 OF 16 MEDLINE
AN 90294401 MEDLINE
TI The **vascular endothelial** cell as a vehicle for **gene therapy**.
SO JOURNAL OF VASCULAR SURGERY, (1990 Jun) 11 (6) 793-8.
Journal code: 8407742. ISSN: 0741-5214.
AU Callow A D
AB Increasing knowledge that has accumulated during the past decade reveals that the endothelial cell plays a far larger role than that traditionally assigned to it, namely maintenance of the fluid state of the blood. Unraveling the complex interreactions of the endothelial cell with the other cellular and molecular components of the arterial wall, as well as with the blood and its cellular and particulate components, is leading to better understanding of anastomotic hyperplasia and recurrent **stenosis** after endarterectomy and balloon angioplasty. More recently with the newly acquired techniques of inserting genetic material into the **vascular endothelial** cell many new therapeutic possibilities may be developed. Important to the technique of seeding vascular grafts, and the possible use of the genetically modified endothelial cell for **gene therapy** systems, are the needs to identify the origin of the cell originally seeded and ways to increase their number. Retroviral vectors and genetically conferred antibiotic resistance provide these means.

L13 ANSWER 9 OF 16 SCISEARCH COPYRIGHT 2002 ISI (R)
AN 97:851435 SCISEARCH
TI Molecular analysis of blood vessel formation and disease
SO AMERICAN JOURNAL OF PHYSIOLOGY-HEART AND CIRCULATORY PHYSIOLOGY, (NOV 1997) Vol. 42, No. 5, pp. H2091-H2104.
Publisher: AMER PHYSIOLOGICAL SOC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814.
ISSN: 0363-6135.
AU Carmeliet P (Reprint); Collen D
AB Blood vessels affect the quality of life in many ways. They provide an essential nutritive function during growth and repair of tissues but, on the other hand, can become affected by disorders or trauma, resulting in bleeding, thrombosis, arterial **stenosis**, and atherosclerosis. Three molecular systems, the **vascular endothelial** growth factor (**VEGF**) system, the plasminogen system, and the coagulation system, have been implicated in the formation and pathobiology of blood vessels. This review focuses on the role of these systems in these processes. Recent gene-targeting studies have identified **VEGF** as a potent modulator of the formation of endothelial cell-lined channels. Somewhat unanticipated, the initiator of coagulation is not only involved in the control of hemostasis but also in the maturation of a muscular wall around the endothelium. With different murine models of cardiovascular disease, a pleiotropic role of the plasminogen system was elucidated in thrombosis, in arterial neointima formation after vascular wound healing and allograft transplantation, in atherosclerosis, and in the formation of atherosclerotic aneurysms. Surprisingly, tissue-type plasminogen activator is also involved in brain damage after ischemic or neurotoxic insults. The insights from these gene-targeting studies have formed the basis for designing **gene therapy** strategies for restenosis and thrombosis, which have been successfully tested in these knockout models.

L13 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2002 ACS
AN 2002:505921 CAPLUS
TI Increased vascularity detected by digital subtraction angiography after **VEGF** gene transfer to human lower limb artery: a randomized, placebo-controlled, double-blinded phase II study
SO Molecular Therapy (2002), 6(1), 127-133
CODEN: MTOHCK; ISSN: 1525-0016
AU Makinen, Kimmo; Manninen, Hannu; Hedman, Marja; Matsi, Pekka; Mussalo, Hanna; Alhava, Esko; Yla-Herttuala, Seppo
AB **Vascular endothelial** growth factor (**VEGF**)

gene therapy may be useful for the treatment of lower-limb ischemia. The objectives of this study were to evaluate safety and angiog. and hemodynamic responses of local catheter-mediated **VEGF gene therapy** in ischemic lower-limb arteries after percutaneous transluminal angioplasty (PTA). For this study, we recruited patients with chronic lower-limb ischemia and atherosclerotic infrainguinal occlusion or **stenosis** suitable for PTA. In the study, 18 patients received 2 .times. 1010 plaque-forming units (pfu) **VEGF**-adenovirus (**VEGF**-Ad), 17 patients received **VEGF**-plasmid/liposome (**VEGF**-P/L; 2000 .mu.g of **VEGF** plasmid, 2000 .mu.l of DOTMA:DOPE), and 19 control patients received Ringer's lactate at the angioplasty site. Digital subtraction angiog. (DSA) was used to evaluate vascularity before, immediately after, and 3 mo after the PTA. Clin. follow-up data, basic lab. tests, and ankle-brachial index (ABI) were evaluated. Primary endpoint was DSA anal. of vascularity, and secondary endpoints were restenosis rate, Rutherford class, and ABI after 3 mo follow-up. No major gene transfer-related side effects or differences in lab. tests were detected between the study groups. However, anti-adenovirus antibodies increased in 61% of the patients treated with **VEGF**-Ad. For the primary endpoint, follow-up DSA revealed increased vascularity in the **VEGF**-treated groups distally to the gene transfer site (**VEGF**-Ad P = 0.03, **VEGF**-P/L P = 0.02) and in the **VEGF**-Ad group in the region of the clin. most severe ischemia (P = 0.01). As for the secondary endpoints, mean Rutherford class and ABI showed statistically significant improvements in the **VEGF**-Ad and **VEGF**-P/L groups, but similar improvements were also seen in the control patients. We conclude that catheter-mediated **VEGF gene therapy** is safe and well tolerated. Angiog. demonstrated that **VEGF** gene transfer increased vascularity after PTA in both **VEGF**-Ad- and **VEGF**-P/L-treated groups.

L13 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2002 ACS
AN 1998:323262 CAPLUS
DN 129:45270
TI Therapeutic use of **vascular endothelial** growth factor and a delivery device for the treatment of intimal hyperplasia
SO PCT Int. Appl., 72 pp.
CODEN: PIXXD2
IN Martin, John Francis; Yla-Herttuala, Seppo; Barker, Stephen George Edward
AB **Vascular endothelial** growth factor (**VEGF**) has utility in the treatment of intimal hyperplasia, hypertension and atherosclerosis, and of conditions susceptible to treatment with agents that produce nitric oxide or prostacyclin. Instead of **VEGF**, an equiv. agent such as an agonist of **VEGF** receptors may be given, as may nucleic acid encoding such an agonist. The agent may successfully be administered via the adventitial surface of a blood vessel, e.g. using a device which defines a reservoir between the body wall and the vessel's adventitial surface, the reservoir being at least part-filled by a pharmaceutical formulation contg. the agent to be delivered.

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9820027	A2	19980514	WO 1997-GB3015	19971103
	WO 9820027	A3	19981008		
	W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9747906	A1	19980529	AU 1997-47906	19971103
	AU 729420	B2	20010201		
	EP 941116	A2	19990915	EP 1997-910563	19971103
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	CN 1240359	A	20000105	CN 1997-180198	19971103
	JP 2001503755	T2	20010321	JP 1998-521140	19971103
	NO 9902106	A	19990630	NO 1999-2106	19990430

KR 2000052999 A 20000825 KR 1999-703881 19990430

=>

(FILE 'HOME' ENTERED AT 14:10:09 ON 15 JUL 2002)

FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, BIOSIS, MEDICONF'
ENTERED AT 14:10:18 ON 15 JUL 2002
E RESTONOSIS
L1 19 S E3
E STENOSIS
L2 183734 S E3
L3 183748 S RESTONOSIS OR STENOSIS
L4 86 S L3 AND VEGF?
L5 55 DUP REM L4 (31 DUPLICATES REMOVED)
L6 55 FOCUS L5 1-
L7 34 S L5 AND (GENE OR DNA OR DEOXY? OR TRANS? OR VIR? OR VECTOR)
E ALITALO KAR?/AU
L8 543 S E5
L9 5 S L8 AND L3
L10 4 DUP REM L9 (1 DUPLICATE REMOVED)
L11 209 S L3 AND (GENE THERAP?)
L12 135 DUP REM L11 (74 DUPLICATES REMOVED)
L13 16 S L12 AND (VEGF? OR (VASCULAR ENDOTHELIAL))

=> d l13 11 all

L13 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2002 ACS
AN 2000:290851 CAPLUS
DN 132:318341
TI Use of **VEGF**-C or **VEGF**-D gene or protein to prevent restenosis
IN Yla-Herttuala, Seppo; Alitalo, Kari; Hiltunen, Mikko O.; Jeltsch, Markku M.; Achen, Marc G.
PA Ludwig Institute for Cancer Research, USA; Helsinki University Licensing Ltd. Oy
SO PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K038-00
CC 2-10 (Mammalian Hormones)
Section cross-reference(s): 3, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000024412	A2	20000504	WO 1999-US24054	19991026
	WO 2000024412	A3	20000803		
	W: AU, CA, CN, JP, NO, NZ				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 1126870	A2	20010829	EP 1999-956559	19991026
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	NO 2001002017	A	20010626	NO 2001-2017	20010424
PRAI	US 1998-105587P	P	19981026		
	WO 1999-US24054	W	19991026		

AB The present invention provides materials and methods for preventing **stenosis** or restenosis of a blood vessel using **Vascular Endothelial** Growth Factor C (**VEGF**-C) and/or **Vascular Endothelial** Growth Factor D (**VEGF**-D) genes or proteins. A medical device designed to contact a surface of a blood vessel in the course of surgery to treat **stenosis** of the blood vessel is also claimed, the device characterized by an improvement comprising integrating into the device a compn. effective to prevent restenosis, said compn. comprising at least one anti-restenosis agent selected from the group consisting of a **VEGF**-C polynucleotide, a **VEGF**-C polypeptide, a **VEGF**-D polynucleotide, and a **VEGF**-D polypeptide. The medical device is selected from the group consisting of intravascular stents, intravascular catheters, extravascular collars, elastomeric membranes adapted to cover a surface of an intravascular stent or catheter, and combinations thereof. Also claimed is a kit for treating restenosis comprising a container holding at least

one anti-restenosis agent of the invention and a label attached to or packaged with the container, the label describing use of the compd. for prevention of restenosis of a blood vessel. The kit further comprises a medical device of the invention.

ST **VEGF** C D therapy restenosis **stenosis**; **gene therapy VEGF** C D restenosis **stenosis**; medical device **VEGF** C D therapy restenosis **stenosis**

IT Artery, disease
(aorta, restenosis; use of **VEGF**-C or **VEGF**-D gene or protein to prevent restenosis and **stenosis**)

IT Medical goods
(catheters; medical devices contg. **VEGF**-C or **VEGF**-D gene or protein to prevent restenosis and **stenosis**)

IT Artery
(coronary, angioplasty; use of **VEGF**-C or **VEGF**-D gene or protein to prevent restenosis and **stenosis**)

IT Membranes, nonbiological
(elastomeric membranes adapted to cover a surface of an intravascular stent or catheter; medical devices contg. **VEGF**-C or **VEGF**-D gene or protein to prevent restenosis and **stenosis**)

IT Medical goods
(extravascular collars; medical devices contg. **VEGF**-C or **VEGF**-D gene or protein to prevent restenosis and **stenosis**)

IT Medical goods
(medical devices contg. **VEGF**-C or **VEGF**-D gene or protein to prevent restenosis and **stenosis**)

IT Artery, disease
(restenosis; use of **VEGF**-C or **VEGF**-D gene or protein to prevent restenosis and **stenosis**)

IT Artery, disease
(**stenosis**; use of **VEGF**-C or **VEGF**-D gene or protein to prevent restenosis and **stenosis**)

IT Medical goods
(stents, coronary stent; medical devices contg. **VEGF**-C or **VEGF**-D gene or protein to prevent restenosis and **stenosis**)

IT Blood vessel, disease
Gene therapy
(use of **VEGF**-C or **VEGF**-D gene or protein to prevent restenosis and **stenosis**)

IT 172000-74-7 203626-13-5 266669-79-8, 3: PN: WO0024412 SEQID: 6 unclaimed DNA 266669-80-1, 4: PN: WO0024412 SEQID: 7 unclaimed DNA 266669-81-2, 5: PN: WO0024412 SEQID: 8 unclaimed DNA 266669-82-3, 6: PN: WO0024412 SEQID: 9 unclaimed DNA 266669-83-4, 7: PN: WO0024412 SEQID: 10 unclaimed DNA 266669-84-5, 8: PN: WO0024412 SEQID: 11 unclaimed DNA 266669-85-6, 9: PN: WO0024412 SEQID: 12 unclaimed DNA 266669-86-7 266669-87-8 266669-88-9 266669-89-0 266669-90-3 266669-91-4, 18: PN: WO0024412 SEQID: 5 unclaimed DNA
RL: PRP (Properties)
(unclaimed nucleotide sequence; use of **VEGF**-C or **VEGF**-D gene or protein to prevent restenosis)

IT 203528-36-3
RL: PRP (Properties)
(unclaimed protein sequence; use of **VEGF**-C or **VEGF**-D gene or protein to prevent restenosis)

IT 173402-52-3 188417-84-7, **Vascular Endothelial** Growth Factor C 193363-12-1, **Vascular Endothelial** Growth Factor D 266354-82-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of **VEGF**-C or **VEGF**-D gene or protein to prevent restenosis and **stenosis**)

IT 173078-95-0
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of **VEGF**-C or **VEGF**-D gene or protein to prevent restenosis and **stenosis**)

```
     (FILE 'HOME' ENTERED AT 14:10:09 ON 15 JUL 2002)

     FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, BIOSIS, MEDICONF'
     ENTERED AT 14:10:18 ON 15 JUL 2002
                E RESTONOSIS
L1           19 S E3
                E STENOSIS
L2       183734 S E3
L3       183748 S RESTONOSIS OR STENOSIS
L4           86 S L3 AND VEGF?
L5           55 DUP REM L4 (31 DUPLICATES REMOVED)
L6           55 FOCUS L5 1-
L7           34 S L5 AND (GENE OR DNA OR DEOXY? OR TRANS? OR VIR? OR VECTOR)
                E ALITALO KAR?/AU
L8          543 S E5
L9            5 S L8 AND L3
L10           4 DUP REM L9 (1 DUPLICATE REMOVED)

=> d an ti so au ab pi l10 1-4

L10  ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2002 ACS
AN   2002:444386  CAPLUS
DN   137:19390
TI   VEGF-C polypeptides, polynucleotides and anti-VEGF-C antibodies for
     diagnosing and treating endothelial or angiogenic diseases
SO   U.S., 71 pp., Cont.-in-part of U.S. 6,245,530.
     CODEN: USXXAM
IN   Alitalo, Kari; Joukov, Vladimir
AB   The invention discloses VEGF-C, a polypeptide ligand for Flt4 receptor
     tyrosine kinase (VEGFR-3), polynucleotides encoding them, and antisense
     oligonucleotides for diagnosis, therapy and drug screening use.  The
     invention also provides monoclonal and polyclonal antibodies that are
     reactive with VEGF-C for diagnostic application to monitor angiogenesis,
     vascularization, lymphatic vessels and their disease states, wound
     healing, or certain hematopoietic or leukemia cells, and for blockade or
     activation of Flt4 receptor.  The ligand and antibody may be coupled to
     supermagnetic , paramagnetic, electron dense, echogenic, or radioactive
     agent for imaging.
     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     --------------    ----  --------       ---------------  --------
PI   US 6403088         B1   20020611       US 1996-601132   19960214
     US 6221839         B1   20010424       US 1995-510133   19950801
     US 6245530         B1   20010612       US 1996-585895   19960112
     CA 2228248         AA   19970213       CA 1996-2228248  19960801
     WO 9705250         A2   19970213       WO 1996-FI427    19960801
     WO 9705250         A3   19970410
         W:  AU, CA, CN, JP, NO, NZ, US
         RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
     AU 9666169         A1   19970226       AU 1996-66169    19960801
     AU 711578          B2   19991014
     EP 842273          A2   19980520       EP 1996-925768   19960801
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
     JP 11510689        T2   19990921       JP 1996-507262   19960801
     WO 9833917         A1   19980806       WO 1998-US1973   19980202
         W:  AU, CA, CN, JP, NZ, US, US, US, US, US, US, US
         RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

L10  ANSWER 2 OF 4  CAPLUS  COPYRIGHT 2002 ACS         DUPLICATE 1
AN   2001:765206  CAPLUS
DN   136:67498
TI   Net-targeted mutant mice develop a vascular phenotype and up-regulate
     egr-1
SO   EMBO Journal (2001), 20(18), 5139-5152
     CODEN: EMJODG; ISSN: 0261-4189
AU   Ayadi, Abdelkader; Zheng, Hong; Sobieszczuk, Peter; Buchwalter, Gilles;
     Moerman, Philippe; Alitalo, Kari; Wasylyk, Bohdan
AB   The ternary complex factors (TCFs) Net, Elk-1 and Sap-1 regulate immediate
     early genes through serum response elements (SREs) in vitro, but,
```

surprisingly, their in vivo roles are unknown. Net is a repressor that is expressed in sites of vasculogenesis during mouse development. We have made gene-targeted mice that express a hypomorphic mutant of Net, Net.delta., which lacks the Ets DNA-binding domain. Strikingly, homozygous mutant mice develop a vascular defect and up-regulate an immediate early gene implicated in vascular disease, egr-1. They die after birth due to respiratory failure, resulting from the accumulation of chyle in the thoracic cage (chylothorax). The mice have dilated lymphatic vessels (lymphangiectasis) as early as E16.5. Interestingly, they express more egr-1 in heart and pulmonary arteries at E18.5. Net neg. regulates the egr-1 promoter and binds specifically to SRE-5. Egr-1 has been assocd. with pathologies involving vascular **stenosis** (e.g. atherosclerosis), and here egr-1 dysfunction could possibly be assocd. with obstructions that ultimately affect the lymphatics. These results show that Net is involved in vascular biol. and egr-1 regulation in vivo.

L10 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2002 ACS
AN 2000:290851 CAPLUS
DN 132:318341
TI Use of VEGF-C or VEGF-D gene or protein to prevent restenosis
SO PCT Int. Appl., 61 pp.
CODEN: PIXXD2
IN Yla-Herttuala, Seppo; **Alitalo, Kari**; Hiltunen, Mikko O.; Jeltsch, Markku M.; Achen, Marc G.
AB The present invention provides materials and methods for preventing **stenosis** or restenosis of a blood vessel using Vascular Endothelial Growth Factor C (VEGF-C) and/or Vascular Endothelial Growth Factor D (VEGF-D) genes or proteins. A medical device designed to contact a surface of a blood vessel in the course of surgery to treat **stenosis** of the blood vessel is also claimed, the device characterized by an improvement comprising integrating into the device a compn. effective to prevent restenosis, said compn. comprising at least one anti-restenosis agent selected from the group consisting of a VEGF-C polynucleotide, a VEGF-C polypeptide, a VEGF-D polynucleotide, and a VEGF-D polypeptide. The medical device is selected from the group consisting of intravascular stents, intravascular catheters, extravascular collars, elastomeric membranes adapted to cover a surface of an intravascular stent or catheter, and combinations thereof. Also claimed is a kit for treating restenosis comprising a container holding at least one anti-restenosis agent of the invention and a label attached to or packaged with the container, the label describing use of the compd. for prevention of restenosis of a blood vessel. The kit further comprises a medical device of the invention.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000024412	A2	20000504	WO 1999-US24054	19991026
WO 2000024412	A3	20000803		
W: AU, CA, CN, JP, NO, NZ				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1126870	A2	20010829	EP 1999-956559	19991026
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NO 2001002017	A	20010626	NO 2001-2017	20010424

L10 ANSWER 4 OF 4 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:106500 BIOSIS
TI Clinical applications of angiogenic growth factors and their inhibitors.
SO Nature Medicine, (Dec., 1999) Vol. 5, No. 12, pp. 1359-1364.
ISSN: 1078-8956.
AU Ferrara, Napoleone (1); **Alitalo, Kari (1)**
AB Promoting the formation of new collateral vessels in ischemic tissues using angiogenic growth factors (therapeutic angiogenesis) is a an exciting frontier of cardiovascular medicine. Conversely, inhibition of the action of key regulators of angiogenesis, such as VEGF, constitutes a promising approach for the treatment of solid tumors and intraocular neovascular syndromes. These concepts are being tested now in clinical trials.

L6 ANSWER 1 OF 55 CAPLUS COPYRIGHT 2002 ACS
AN 2000:290851 CAPLUS
DN 132:318341
TI Use of **VEGF**-C or **VEGF**-D gene or protein to prevent restenosis
SO PCT Int. Appl., 61 pp.
CODEN: PIXXD2
IN Yla-Herttuala, Seppo; Alitalo, Kari; Hiltunen, Mikko O.; Jeltsch, Markku M.; Achen, Marc G.
AB The present invention provides materials and methods for preventing **stenosis** or restenosis of a blood vessel using Vascular Endothelial Growth Factor C (**VEGF**-C) and/or Vascular Endothelial Growth Factor D (**VEGF**-D) genes or proteins. A medical device designed to contact a surface of a blood vessel in the course of surgery to treat **stenosis** of the blood vessel is also claimed, the device characterized by an improvement comprising integrating into the device a compn. effective to prevent restenosis, said compn. comprising at least one anti-restenosis agent selected from the group consisting of a **VEGF**-C polynucleotide, a **VEGF**-C polypeptide, a **VEGF**-D polynucleotide, and a **VEGF**-D polypeptide. The medical device is selected from the group consisting of intravascular stents, intravascular catheters, extravascular collars, elastomeric membranes adapted to cover a surface of an intravascular stent or catheter, and combinations thereof. Also claimed is a kit for treating restenosis comprising a container holding at least one anti-restenosis agent of the invention and a label attached to or packaged with the container, the label describing use of the compd. for prevention of restenosis of a blood vessel. The kit further comprises a medical device of the invention.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000024412	A2	20000504	WO 1999-US24054	19991026
WO 2000024412	A3	20000803		
W: AU, CA, CN, JP, NO, NZ				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1126870	A2	20010829	EP 1999-956559	19991026
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NO 2001002017	A	20010626	NO 2001-2017	20010424

L6 ANSWER 2 OF 55 CAPLUS COPYRIGHT 2002 ACS
AN 1997:63042 CAPLUS
DN 126:129592
TI The function and application of vascular endothelial growth factor
SO Shengli Kexue Jinzhan (1996), 27(3), 255-257
CODEN: SLKHA8; ISSN: 0559-7765
AU Zhang, Man; Zhou, Airu
AB A review with 10 refs. on the function and application of vascular endothelial growth factor (**VEGF**) with subdivision headings (1) **VEGF** and vascular re-**stenosis**; (2) **VEGF** and coronary ischemia; (3) **VEGF** and hindlimb ischemia; (4) **VEGF** and embryonic development; (5) **VEGF** and retinal neovascularization; (6) **VEGF** and rheumatoid arthritis and (7) **VEGF** and tumor.

L6 ANSWER 3 OF 55 CAPLUS COPYRIGHT 2002 ACS
AN 2002:505921 CAPLUS
TI Increased vascularity detected by digital subtraction angiography after **VEGF** gene transfer to human lower limb artery: a randomized, placebo-controlled, double-blinded phase II study
SO Molecular Therapy (2002), 6(1), 127-133
CODEN: MTOHCK; ISSN: 1525-0016
AU Makinen, Kimmo; Manninen, Hannu; Hedman, Marja; Matsi, Pekka; Mussalo, Hanna; Alhava, Esko; Yla-Herttuala, Seppo
AB Vascular endothelial growth factor (**VEGF**) gene therapy may be useful for the treatment of lower-limb ischemia. The objectives of this study were to evaluate safety and angiog. and hemodynamic responses of local catheter-mediated **VEGF** gene therapy in ischemic lower-limb arteries after percutaneous transluminal angioplasty (PTA). For this study, we recruited patients with chronic lower-limb ischemia and atherosclerotic infrainguinal occlusion or **stenosis** suitable for PTA. In the study, 18 patients received 2 .times. 1010 plaque-forming units (pfu) **VEGF**-adenovirus (**VEGF**-Ad), 17 patients received **VEGF**-plasmid/liposome (**VEGF**-P/L; 2000 .mu.g of **VEGF** plasmid, 2000 .mu.l of DOTMA:DOPE), and 19 control patients received Ringer's lactate at the angioplasty site. Digital subtraction angiog. (DSA) was used to evaluate vascularity before, immediately after, and 3 mo after the PTA. Clin. follow-up data, basic lab. tests, and ankle-brachial index (ABI) were evaluated. Primary endpoint was DSA anal. of vascularity, and secondary endpoints were restenosis rate, Rutherford class, and ABI after 3 mo follow-up. No major gene transfer-related side effects or differences in lab. tests were detected between the study groups. However, anti-adenovirus antibodies increased in 61% of the patients treated with **VEGF**-Ad. For the primary endpoint, follow-up DSA revealed increased vascularity in the **VEGF**-treated groups distally to the gene transfer site (**VEGF**-Ad P = 0.03, **VEGF**-P/L P = 0.02) and in the **VEGF**-Ad group in the region of the clin. most severe ischemia (P = 0.01). As for the secondary endpoints, mean Rutherford class and ABI showed statistically significant improvements in the **VEGF**-Ad and **VEGF**-P/L groups, but similar improvements were also seen in the control patients. We conclude that catheter-mediated **VEGF** gene therapy is safe and well tolerated. Angiog. demonstrated that **VEGF** gene transfer increased vascularity after PTA in both **VEGF**-Ad- and **VEGF**-P/L-treated groups.

L6 ANSWER 4 OF 55 CAPLUS COPYRIGHT 2002 ACS
AN 2002:444386 CAPLUS
DN 137:19390
TI **VEGF**-C polypeptides, polynucleotides and anti-**VEGF**-C antibodies for diagnosing and treating endothelial or angiogenic diseases
SO U.S., 71 pp., Cont.-in-part of U.S. 6,245,530.
CODEN: USXXAM
IN Alitalo, Kari; Joukov, Vladimir
AB The invention discloses **VEGF**-C, a polypeptide ligand for Flt4 receptor tyrosine kinase (**VEGFR**-3), polynucleotides encoding them, and antisense oligonucleotides for diagnosis, therapy and drug screening use. The invention also provides monoclonal and polyclonal antibodies that are reactive with **VEGF**-C for diagnostic application to monitor angiogenesis, vascularization, lymphatic vessels and their disease states, wound healing, or certain hematopoietic or leukemia cells, and for blockade or activation of Flt4 receptor. The ligand and antibody may be coupled to supermagnetic , paramagnetic, electron dense, echogenic, or radioactive agent for imaging.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 6403088	B1	20020611	US 1996-601132	19960214
US 6221839	B1	20010424	US 1995-510133	19950801
US 6245530	B1	20010612	US 1996-585895	19960112
CA 2228248	AA	19970213	CA 1996-2228248	19960801
WO 9705250	A2	19970213	WO 1996-FI427	19960801
WO 9705250	A3	19970410		
W: AU, CA, CN, JP, NO, NZ, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9666169	A1	19970226	AU 1996-66169	19960801
AU 711578	B2	19991014		
EP 842273	A2	19980520	EP 1996-925768	19960801
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11510689	T2	19990921	JP 1996-507262	19960801
WO 9833917	A1	19980806	WO 1998-US1973	19980202
W: AU, CA, CN, JP, NZ, US, US, US, US, US, US, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				

L6 ANSWER 5 OF 55 CAPLUS COPYRIGHT 2002 ACS
AN 2000:13779 CAPLUS
DN 133:15649
TI The role of vascular endothelial growth factor in vein graft **stenosis**, carotid and aortic atherosclerotic disease
SO Surgical Forum (1998), 49, 318-320
CODEN: SUFOAX; ISSN: 0071-8041
AU Henderson, Aphrodite M.; Hunter, Glenn C.
AB Vascular endothelial growth factor (**VEGF**) expression has been implicated in the formation of new blood vessels in the developing embryo, wound healing, myocardial ischemia, atherosclerosis, rheumatoid arthritis, diabetic retinopathy, and tumorigenesis. Inflammatory cells, smooth muscle cells, fibroblasts, microvessels, and extracellular matrix are well-recognized components of atherosclerotic plaque and restenotic lesions. In the present study, we analyzed atherosclerotic tissue from patients undergoing carotid endarterectomy and aortic resection. **VEGF** expression was most prominent in stenotic vein grafts and almost completely absent in those specimens showing both myointimal thickening and atherosclerosis.

L7 ANSWER 2 OF 34 MEDLINE
AN 2002046300 MEDLINE
TI Simultaneous surgical revascularization and angiogenic **gene** therapy in diffuse coronary artery disease.
SO EUROPEAN JOURNAL OF CARDIO-THORACIC SURGERY, (2001 Dec) 20 (6) 1128-34. Journal code: 8804069. ISSN: 1010-7940.
AU Huwer H; Welter C; Ozbek C; Seifert M; Straub U; Greilach P; Kalweit G; Isringhaus H
AB OBJECTIVE: The cytokine vascular endothelial growth factor (**VEGF**) is capable of triggering angiogenesis and at higher concentrations vasculogenesis. We report on a pilot study where **VEGF-DNA** as an additional therapy to coronary artery bypass grafting was injected into the myocardium in 24 patients (pts) with proximal coronary artery **stenosis** and diffuse peripheral disease. One region of the myocardium with proven ischemia remained unsupplied after surgery because the respective epicardial coronary artery was not graftable. METHODS AND RESULTS: Plasmid **DNA** encoding for the 165- and 167-amino acid isoform of the human **VEGF genes** was injected directly into the myocardium, not amenable to surgical revascularization at a dosage of 1000 microg each, using a standardized protocol. A (99m)Tc-sestamibi-SPECT at rest performed 7 days prior to the operation, had shown decreased marker activity in the region of interest. Controls were made 1 week and 80-100 days postoperatively. **Transmural** scarring was ruled out intraoperatively. Coronary and left ventricular angiographies were performed preoperatively and 3 months postsurgery, respectively. One or more of the following angiographic items were found in 16/24 patients postoperatively. (1) Improvement of regional left ventricular function at the **VEGF** treated myocardial sector (5/24 pts). (2) Newly visible vessels considered as collaterals (8/24 pts). (3) Earlier filling of parent vessels (6/24 pts). (4) An increase in diameter of preoperatively existing collateral vessels (7/24). An increased perfusion at rest in the region of **gene** application was detected in 3/24 patients by early postoperative (99m)Tc-sestamibi-SPECT investigation. In six additional cases, local perfusion increased markedly until the late examination. No perioperative myocardial infarctions and no signs of inflammation were observed. Newly developed abnormal vasculature was not detected in any patient. CONCLUSIONS: Direct intramyocardial administration of **VEGF**(165)-**DNA** and **VEGF**(167)-**DNA** may result occasionally in an enhancement of collateral vascularization in regions with diffuse peripheral coronary artery disease not surgically amenable. During midterm follow-up no adverse effects of **VEGF-DNA** application are observed so far. The very slight midterm improvements caused us to stop further **VEGF-DNA** application and, in our opinion, do not justify a prospective, and randomized study with a control group.

L7 ANSWER 3 OF 34 MEDLINE
AN 2001681674 MEDLINE
TI Clinical protocol. A phase IIb, randomized, multicenter, double-blind study of the efficacy and safety of Trinam (EG004) in **stenosis** prevention at the graft-vein anastomosis site in dialysis patients.
SO HUMAN GENE THERAPY, (2001 Nov 1) 12 (16) 2025-7.
Journal code: 9008950. ISSN: 1043-0342.
AU Fuster V; Charlton P; Boyd A
AB Hemodialysis access complications remain a major cause of morbidity for patients with end-stage renal disease who are undergoing chronic hemodialysis. Vascular access complications occur in approximately 40% of patients with polytetrafluorethylene (PTFE) grafts within the first 6 months, primarily due to **stenosis** and thrombosis. Thrombosis at the site of vascular access increases the risk of infection and the need for hospitalization, and may lead to loss of potential new sites for vascular access. To a large extent, the failure of hemodialysis access is due to the rapid development of an intimal hyperplastic lesion in the region of anastomosis between the PTFE graft and the vein. The hospital costs related to hemodialysis access procedures are estimated to be around $1.3 billion per year and the total cost of hemodialysis complications to the US healthcare system is thought to be in excess of $2 billion per year. Ark Therapeutics Ltd. are developing a vascular endothelial growth factor D (**VEGF**-D) **gene** in an adenoviral **vector** which is delivered locally to the adventitial surface of a graft-vein anastomosis by means of a collagen collar device. The proposed indication for this product (Trinam) is the prevention of intimal hyperplasia at the graft-vein anastomosis site in patients who require vascular access to facilitate hemodialysis for end-stage renal disease. The rationale for Trinam to prevent intimal hyperplasia at the graft-vein anastomosis follows the discovery that **VEGF** has a 'vasculoprotective' action, resulting in inhibition of smooth muscle cell migration and proliferation. The fundamental mechanism for this vasculoprotective effect of **VEGF**, as distinct from its more widely appreciated 'angiogenic' role, is that **VEGF** acts on surface receptors on endothelial cells resulting in increased production of nitric oxide and prostacyclin. These entities diffuse into the media of the blood vessel wall and counter the tendency for intimal hyperplasia to develop. In an in vivo rabbit model of intimal thickening in carotid arteries, adventitial delivery of **VEGF** using a silastic collar as a **gene** delivery reservoir prevented smooth muscle cell proliferation without evidence of new blood vessel formation, indicating that the mechanism by which **VEGF** inhibited intimal hyperplasia did not involve angiogenesis. The objective of the proposed study is to assess the efficacy and safety of local delivery of Trinam when applied to the graft-vein anastomosis site in patients with end-stage renal disease who require vascular access for hemodialysis. At the time of surgical placement of a PTFE arm graft, patients will be randomized to either a single administration of Trinam or to 'no treatment' (i.e., control group). It is hypothesised that Trinam administration will result in less **stenosis** at the graft-vein anastomosis site (as measured by fistulography) compared with controls and therefore will reduce the need for interventions in dialysis patients. Approximately 210 patients will be enrolled from 10-15 centers and patients will be evaluated for efficacy and safety over 6 months. The total dose of Trinam will be 1 x 10(11) **viral** particles (replication-deficient adenoviral **vector**). This dose of Trinam was not associated with any significant toxicology findings in a preclinical study of pigs in which a PTFE loop-graft was anastomosed from the carotid artery to the internal jugular vein to mimic hemodialysis vascular access surgery.

L7 ANSWER 5 OF 34 MEDLINE
AN 2000507205 MEDLINE
TI Intravascular adenovirus-mediated **VEGF**-C **gene transfer** reduces neointima formation in balloon-denuded rabbit aorta.
SO CIRCULATION, (2000 Oct 31) 102 (18) 2262-8.
Journal code: 0147763. ISSN: 1524-4539.
AU Hiltunen M O; Laitinen M; Turunen M P; Jeltsch M; Hartikainen J; Rissanen T T; Laukkanen J; Niemi M; Kossila M; Hakkinen T P; Kivela A; Enholm B; Mansukoski H; Turunen A M; Alitalo K; Yla-Herttuala S
AB BACKGROUND: **Gene transfer** to the vessel wall may provide new possibilities for the treatment of vascular disorders, such as postangioplasty restenosis. In this study, we analyzed the effects of adenovirus-mediated vascular endothelial growth factor (**VEGF**)-C **gene transfer** on neointima formation after endothelial denudation in rabbits. For comparison, a second group was treated with **VEGF**-A adenovirus and a third group with lacZ adenovirus. Clinical-grade adenoviruses were used for the study. METHODS AND RESULTS: Aortas of cholesterol-fed New Zealand White rabbits were balloon-denuded, and **gene transfer** was performed 3 days later. Animals were euthanized 2 and 4 weeks after the **gene transfer**, and intima/media ratio (I/M), histology, and cell proliferation were analyzed. Two weeks after the **gene transfer**, I/M in the lacZ-**transfected** control group was 0. 57+/-0.04. **VEGF**-C **gene transfer** reduced I/M to 0.38+/-0.02 (P:<0.05 versus lacZ group). I/M in **VEGF**-A-treated animals was 0.49+/-0.17 (P:=NS). The tendency that both **VEGF** groups had smaller I/M persisted at the 4-week time point, when the lacZ group had an I/M of 0.73+/-0.16, the **VEGF**-C group 0.44+/-0.14, and the **VEGF**-A group 0. 63+/-0.21 (P:=NS). Expression of **VEGF** receptors 1, 2, and 3 was detected in the vessel wall by immunocytochemistry and in situ hybridization. As an additional control, the effect of adenovirus on cell proliferation was analyzed by performing **gene transfer** to intact aorta without endothelial denudation. No differences were seen in smooth muscle cell proliferation or I/M between lacZ adenovirus and 0.9% saline-treated animals. CONCLUSIONS: Adenovirus-mediated **VEGF**-C **gene transfer** may be useful for the treatment of postangioplasty restenosis and vessel wall thickening after vascular manipulations.

L7 ANSWER 6 OF 34 MEDLINE
AN 2000143033 MEDLINE
TI Catheter-mediated vascular endothelial growth factor **gene transfer** to human coronary arteries after angioplasty.
SO HUMAN GENE THERAPY, (2000 Jan 20) 11 (2) 263-70.
Journal code: 9008950. ISSN: 1043-0342.
AU Laitinen M; Hartikainen J; Hiltunen M O; Eranen J; Kiviniemi M; Narvanen O; Makinen K; Manninen H; Syvanne M; Martin J F; Laakso M; Yla-Herttuala S
AB Blood vessels are among the easiest targets for **gene** therapy. However, no data are available about the safety and feasibility of intracoronary **gene transfer** in humans. We studied the safety and efficacy of catheter-mediated vascular endothelial growth factor (**VEGF**) plasmid/liposome (P/L) **gene transfer** in human coronary arteries after percutaneous **translumenal** coronary angioplasty (PTCA) in a randomized, double-blinded, placebo-controlled study. The optimized angioplasty/**gene** delivery method was previously shown to lead to detectable **VEGF gene** expression in human peripheral arteries as analyzed from amputated leg samples. **Gene transfer** to coronary arteries was done with a perfusion-infusion catheter, using 1000 microg of **VEGF** or beta-galactosidase plasmid complexed with 1000 microl of DOTMA:DOPE liposomes. Ten patients received **VEGF** P/L, three patients received beta-galactosidase P/L, and two patients received Ringer lactate. **Gene transfer** to coronary arteries was feasible and well tolerated. Except for a slight increase in serum C-reative protein in all study groups, no adverse effects or abnormalities in laboratory parameters were detected. No **VEGF** plasmid or recombinant **VEGF** protein was present in the systemic circulation after the **gene transfer**. In control angiography 6 months later, no differences were detected in the degree of coronary **stenosis** between treatment and control groups. We conclude that catheter-mediated intracoronary **gene transfer** performed after angioplasty is safe and well tolerated and potentially applicable for the prevention of restenosis and myocardial ischemia.

L7 ANSWER 12 OF 34 CAPLUS COPYRIGHT 2002 ACS
AN 2002:505921 CAPLUS
TI Increased vascularity detected by digital subtraction angiography after **VEGF gene transfer** to human lower limb artery: a randomized, placebo-controlled, double-blinded phase II study
SO Molecular Therapy (2002), 6(1), 127-133
CODEN: MTOHCK; ISSN: 1525-0016
AU Makinen, Kimmo; Manninen, Hannu; Hedman, Marja; Matsi, Pekka; Mussalo, Hanna; Alhava, Esko; Yla-Herttuala, Seppo
AB Vascular endothelial growth factor (**VEGF**) **gene** therapy may be useful for the treatment of lower-limb ischemia. The objectives of this study were to evaluate safety and angiog. and hemodynamic responses of local catheter-mediated **VEGF gene** therapy in ischemic lower-limb arteries after percutaneous **transluminal** angioplasty (PTA). For this study, we recruited patients with chronic lower-limb ischemia and atherosclerotic infrainguinal occlusion or **stenosis** suitable for PTA. In the study, 18 patients received 2 .times. 1010 plaque-forming units (pfu) **VEGF**-adenovirus (**VEGF**-Ad), 17 patients received **VEGF**-plasmid/liposome (**VEGF**-P/L; 2000 .mu.g of **VEGF** plasmid, 2000 .mu.l of DOTMA:DOPE), and 19 control patients received Ringer's lactate at the angioplasty site. Digital subtraction angiog. (DSA) was used to evaluate vascularity before, immediately after, and 3 mo after the PTA. Clin. follow-up data, basic lab. tests, and ankle-brachial index (ABI) were evaluated. Primary endpoint was DSA anal. of vascularity, and secondary endpoints were restenosis rate, Rutherford class, and ABI after 3 mo follow-up. No major **gene transfer**-related side effects or differences in lab. tests were detected between the study groups. However, anti-adenovirus antibodies increased in 61% of the patients treated with **VEGF**-Ad. For the primary endpoint, follow-up DSA revealed increased vascularity in the **VEGF**-treated groups distally to the **gene transfer** site (**VEGF**-Ad P = 0.03, **VEGF**-P/L P = 0.02) and in the **VEGF**-Ad group in the region of the clin. most severe ischemia (P = 0.01). As for the secondary endpoints, mean Rutherford class and ABI showed statistically significant improvements in the **VEGF**-Ad and **VEGF**-P/L groups, but similar improvements were also seen in the control patients. We conclude that catheter-mediated **VEGF gene** therapy is safe and well tolerated. Angiog. demonstrated that **VEGF gene transfer** increased vascularity after PTA in both **VEGF**-Ad- and **VEGF**-P/L-treated groups.

L7 ANSWER 13 OF 34 CAPLUS COPYRIGHT 2002 ACS
AN 2002:444386 CAPLUS
DN 137:19390
TI **VEGF**-C polypeptides, polynucleotides and anti-**VEGF**-C antibodies for diagnosing and treating endothelial or angiogenic diseases
SO U.S., 71 pp., Cont.-in-part of U.S. 6,245,530.
CODEN: USXXAM
IN Alitalo, Kari; Joukov, Vladimir
AB The invention discloses **VEGF**-C, a polypeptide ligand for Flt4 receptor tyrosine kinase (**VEGFR**-3), polynucleotides encoding them, and antisense oligonucleotides for diagnosis, therapy and drug screening use. The invention also provides monoclonal and polyclonal antibodies that are reactive with **VEGF**-C for diagnostic application to monitor angiogenesis, vascularization, lymphatic vessels and their disease states, wound healing, or certain hematopoietic or leukemia cells, and for blockade or activation of Flt4 receptor. The ligand and antibody may be coupled to supermagnetic , paramagnetic, electron dense, echogenic, or radioactive agent for imaging.

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6403088	B1	20020611	US 1996-601132	19960214
	US 6221839	B1	20010424	US 1995-510133	19950801
	US 6245530	B1	20010612	US 1996-585895	19960112
	CA 2228248	AA	19970213	CA 1996-2228248	19960801
	WO 9705250	A2	19970213	WO 1996-FI427	19960801
	WO 9705250	A3	19970410		
	W: AU, CA, CN, JP, NO, NZ, US				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9666169	A1	19970226	AU 1996-66169	19960801
	AU 711578	B2	19991014		
	EP 842273	A2	19980520	EP 1996-925768	19960801
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 11510689	T2	19990921	JP 1996-507262	19960801
	WO 9833917	A1	19980806	WO 1998-US1973	19980202
	W: AU, CA, CN, JP, NZ, US, US, US, US, US, US, US				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				

L7 ANSWER 18 OF 34 CAPLUS COPYRIGHT 2002 ACS
AN 2000:290851 CAPLUS
DN 132:318341
TI Use of **VEGF**-C or **VEGF**-D **gene** or protein to prevent restenosis
SO PCT Int. Appl., 61 pp.
CODEN: PIXXD2
IN Yla-Herttuala, Seppo; Alitalo, Kari; Hiltunen, Mikko O.; Jeltsch, Markku M.; Achen, Marc G.
AB The present invention provides materials and methods for preventing **stenosis** or restenosis of a blood vessel using Vascular Endothelial Growth Factor C (**VEGF**-C) and/or Vascular Endothelial Growth Factor D (**VEGF**-D) **genes** or proteins. A medical device designed to contact a surface of a blood vessel in the course of surgery to treat **stenosis** of the blood vessel is also claimed, the device characterized by an improvement comprising integrating into the device a compn. effective to prevent restenosis, said compn. comprising at least one anti-restenosis agent selected from the group consisting of a **VEGF**-C polynucleotide, a **VEGF**-C polypeptide, a **VEGF**-D polynucleotide, and a **VEGF**-D polypeptide. The medical device is selected from the group consisting of intravascular stents, intravascular catheters, extravascular collars, elastomeric membranes adapted to cover a surface of an intravascular stent or catheter, and combinations thereof. Also claimed is a kit for treating restenosis comprising a container holding at least one anti-restenosis agent of the invention and a label attached to or packaged with the container, the label describing use of the compd. for prevention of restenosis of a blood vessel. The kit further comprises a medical device of the invention.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000024412	A2	20000504	WO 1999-US24054	19991026
WO 2000024412	A3	20000803		
W: AU, CA, CN, JP, NO, NZ				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1126870	A2	20010829	EP 1999-956559	19991026
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NO 2001002017	A	20010626	NO 2001-2017	20010424

L7 ANSWER 22 OF 34 CAPLUS COPYRIGHT 2002 ACS
AN 1998:323262 CAPLUS
DN 129:45270
TI Therapeutic use of vascular endothelial growth factor and a delivery device for the treatment of intimal hyperplasia
SO PCT Int. Appl., 72 pp.
CODEN: PIXXD2
IN Martin, John Francis; Yla-Herttuala, Seppo; Barker, Stephen George Edward
AB Vascular endothelial growth factor (**VEGF**) has utility in the treatment of intimal hyperplasia, hypertension and atherosclerosis, and of conditions susceptible to treatment with agents that produce nitric oxide or prostacyclin. Instead of **VEGF**, an equiv. agent such as an agonist of **VEGF** receptors may be given, as may nucleic acid encoding such an agonist. The agent may successfully be administered via the adventitial surface of a blood vessel, e.g. using a device which defines a reservoir between the body wall and the vessel's adventitial surface, the reservoir being at least part-filled by a pharmaceutical formulation contg. the agent to be delivered.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9820027	A2	19980514	WO 1997-GB3015	19971103
WO 9820027	A3	19981008		
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9747906	A1	19980529	AU 1997-47906	19971103
AU 729420	B2	20010201		
EP 941116	A2	19990915	EP 1997-910563	19971103
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1240359	A	20000105	CN 1997-180198	19971103
JP 2001503755	T2	20010321	JP 1998-521140	19971103
NO 9902106	A	19990630	NO 1999-2106	19990430
KR 2000052999	A	20000825	KR 1999-703881	19990430

L7 ANSWER 23 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:320150 BIOSIS
TI Cytokine expression in a pig model of venous **stenosis** in arteriovenous PTFE grafts.
SO Journal of the American Society of Nephrology, (September, 2001) Vol. 12, No. Program and Abstract Issue, pp. 291A. http://www.jasn.org/. print.
Meeting Info.: ASN (American Society of Nephrology)/ISN (International Society of Nephrology) World Congress of Nephrology San Francisco, CA, USA October 10-17, 2001
ISSN: 1046-6673.
AU Kelly, Burnett (1); Heffelfinger, Sue (1); Miller, MaryAnn (1); Reaves, Anita (1); Armstrong, Janice (1); Roy-Chaudhury, Prabir (1)

L7 ANSWER 24 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:274892 BIOSIS
TI **VEGF gene transfer** to human lower limb artery. A placebo-controlled, randomized, double-blinded phase II study.
SO Circulation, (October 23, 2001) Vol. 104, No. 17 Supplement, pp. II.253. http://circ.ahajournals.org/. print.
Meeting Info.: Scientific Sessions 2001 of the American Heart Association Anaheim, California, USA November 11-14, 2001
ISSN: 0009-7322.
AU Makinen, Kimmo (1); Manninen, Hannu (1); Hedman, Marja (1); Matsi, Pekka (1); Mussalo, Hanna (1); Alhava, Esko (1); Yla-Herttuala, Seppo (1)

L7 ANSWER 25 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:263370 BIOSIS
TI Therapeutic angiogenesis in pigs with chronic myocardial ischemia using Ad-**VEGF165 gene** injections does not require localization to the ischemic zone.
SO Circulation, (October 23, 2001) Vol. 104, No. 17 Supplement, pp. II.69. http://circ.ahajournals.org/. print.
Meeting Info.: Scientific Sessions 2001 of the American Heart Association Anaheim, California, USA November 11-14, 2001
ISSN: 0009-7322.
AU Ueno, Takafumi (1); Kontos, Christopher D.; Annex, Brian H.; Cui, Jianhua; Frohwein, Stephen; Palasis, Maria; Robinson, Keith A.; Chronos, Nicolas A. F.

L7 ANSWER 26 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:224658 BIOSIS
TI External beam radiation (EBR) reduces venous neointimal hyperplasia (VNH) in PTFE dialysis grafts.
SO Journal of the American Society of Nephrology, (September, 2000) Vol. 11, No. Program and Abstract Issue, pp. 187A. http://www.jasn.org/. print.
Meeting Info.: 33rd Annual Meeting of the American Society of Nephrology and the 2000 Renal Week Toronto, Ontario, Canada October 10-16, 2000
ISSN: 1046-6673.
AU Kelly, Burnett S. (1); Heffelfinger, Sue C. (1); Narayana, Ashwath (1); Miller, Mary Ann (1); Nanayakkara, Nuwan (1); Armstrong, Janice (1); Whiting, James F. (1); Roy-Chaudhury, Prabir (1)

L7 ANSWER 27 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:69782 BIOSIS
TI FGFb, **VEGF** and ET-1 levels in human left ventricular hypertrophy. Response to stress.
SO European Heart Journal, (September, 2001) Vol. 22, No. Abstract Supplement, pp. 52. print.
Meeting Info.: XXIII Congress of the European Society of Cardiology together with the 36th Annual General Meeting of the Association for European Paediatric Cardiology Stockholm, Sweden September 01-05, 2001
ISSN: 0195-668X.
AU Maceira, A. M. (1); Cosin-Sales, J. (1); Macias, A. (1); Gavira, J. J. (1); Calabuig, J. (1); Rabago, G.; Martinez-Caro, D. (1); Garcia-Bolao, J. I. (1)

L7 ANSWER 28 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:38886 BIOSIS
TI Plasmatic markers of chronic versus acute myocardial ischaemia: Fibroblast growth factor basic and endothelin-1. Experimental longitudinal study.

SO European Heart Journal, (September, 2001) Vol. 22, No. Abstract Supplement, pp. 158. print.
Meeting Info.: XXIII Congress of the European Society of Cardiology together with the 36th Annual General Meeting of the Association for European Paediatric Cardiology Stockholm, Sweden September 01-05, 2001
ISSN: 0195-668X.
AU Maceira, A. M. (1); Cosin-Sales, J. (1); Rabago, G.; Rodriguez, J. A.; Martinez-Caro, D. (1)

L7 ANSWER 29 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:196292 BIOSIS
TI Intramyocardial levels of vascular endothelial growth factor (**VEGF**) are reduced in a porcine model of hibernating myocardium.
SO Journal of the American College of Cardiology, (February, 2001) Vol. 37, No. 2 Supplement A, pp. 367A. print.
Meeting Info.: 50th Annual Scientific Session of the American College of Cardiology Orlando, Florida, USA March 18-21, 2001
ISSN: 0735-1097.
AU Domkowski, Patrick W. (1); Biswas, Shankha S.; Diodato, Luis H.; Pippen, Anne M.; Thompson, Michael A.; Landolfo, Kevin P.; Annex, Brian H.

L7 ANSWER 30 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:194230 BIOSIS
TI Pharmacokinetics and efficacy of intravenous Vascular Endothelial Growth Factor (rhVEGF) in porcine hibernating myocardium.
SO Journal of the American College of Cardiology, (February, 2001) Vol. 37, No. 2 Supplement A, pp. 338A. print.
Meeting Info.: 50th Annual Scientific Session of the American College of Cardiology Orlando, Florida, USA March 18-21, 2001
ISSN: 0735-1097.
AU Biswas, Shankha S. (1); Domkowski, Patrick W. (1); Diodato, Luis H. (1); Pippen, Anne M. (1); Landolfo, Kevin P. (1); Annex, Brian H. (1)

L7 ANSWER 31 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:149093 BIOSIS
TI Laser therapy in combination with **VEGF**-cDNA in a model of chronic myocardial ischemia.
SO Circulation, (October 31, 2000) Vol. 102, No. 18 Supplement, pp. II.736. print.
Meeting Info.: Abstracts from Scientific Sessions 2000 New Orleans, Louisiana, USA November 12-15, 2000
ISSN: 0009-7322.
AU Lutter, Georg (1); Dern, Peter (1); Attmann, Tim (1); Handke, Michael (1); Ameer, Kim (1); Schreiber, Jeannette (1); Martin, Juergen (1); Marme, Dieter (1); Beyersdorf, Friedhelm (1)

L7 ANSWER 32 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:34371 BIOSIS
TI External beam radiation reduces venous neointimal hyperplasia in PTFE dialysis grafts.
SO International Journal of Radiation Oncology Biology Physics, (2000) Vol. 48, No. 3 Supplement, pp. 183. print.
Meeting Info.: 42nd Annual Meeting of the American Society for Therapeutic Radiology and Oncology Boston, Massachusets, USA October 22-26, 2000 American Society for Therapeutic Radiology and Oncology
. ISSN: 0360-3016.
AU Kelly, B. S. (1); Heffelfinger, S. C. (1); Miller, M. A. (1); Nanayakkara, N. (1); Whiting, J. F. (1); Alexander, J. W. (1); Roy-Chaudhury, P. (1); Narayana, A. (1)

L7 ANSWER 33 OF 34 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:34704 BIOSIS
TI Catheter-mediated **VEGF gene transfer** to human lower limb arteries after PTA.
SO Circulation, (Nov. 2, 1999) Vol. 110, No. 18 SUPPL., pp. I.770.
Meeting Info.: 72nd Scientific Sessions of the American Heart Association Atlanta, Georgia, USA November 7-10, 1999
ISSN: 0009-7322.
AU Makinen, Kimmo (1); Laitinen, Marja; Manninen, Hannu; Matsi, Pekka; Alhava, Esko; Yla-Herttuala, Seppo

L7 ANSWER 34 OF 34 MEDICONF COPYRIGHT 2002 FAIRBASE
AN 14802297 MEDICONF
MT Restenosis European Summit

=>